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Volume V

ANESTHESIOLOGY

August 1976

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USAF SCHOOL OF AEROSPACE MEDICINE
Aerospace Medical Division (AFSC)
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NOTICES

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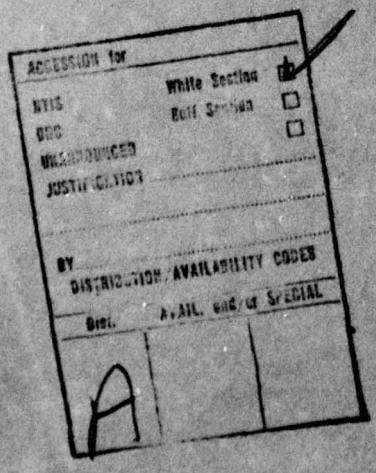

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This review discusses the pharmacology of anesthetic agents and the principles and technics for their administration in laboratory animals.

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PREFACE

This is one of a series of Aeromedical Reviews entitled "Selected Topics in Laboratory Animal Medicine." These publications contain information on the care and use of animals in biomedical research; they are intended for veterinary educators, managers of animal colonies, and individuals who use animals in scientific investigations. The information in these reviews was initially presented as lectures and handouts in the Laboratory Animal Medicine Residency, the Veterinary Surgery Residency, and the annual symposia on Current Trends in Laboratory Animal Medicine. The authors are veterinarians who are specialists in the respective fields of laboratory animal medicine, pathology, toxicology, and surgery. With few exceptions, the authors are graduates of the Laboratory Animal Medicine Residency conducted at the USAF School of Aerospace Medicine and are certified by specialty boards in their chosen field.

Special recognition is due the consulting editors: Col Ralph F. Ziegler, Lt Col Harold W. Casey, Lt Col Gale D. Taylor, and Maj George W. Irving III.

This work was directed and coordinated by the staff of the Veterinary Education Branch, Education Division, USAF School of Aerospace Medicine, Brooks Air Force Base, Texas.

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SELECTED TOPICS IN LABORATORY ANIMAL MEDICINE

VOLUME V ANESTHESIOLOGY

INTRODUCTION

Anesthetic agents have many uses: restraint of animals to enable examination and treatment, surgery, convulsion control, and euthanasia. This review is primarily concerned with the anesthetic agents, equipment, and technics used for laboratory animals.

The laboratory animal veterinarian or research investigator using anesthetics is encouraged to study in detail the pharmacological actions of anesthetic agents and related drugs before using them in animals assigned to research projects. Pharmacology texts should be consulted, with special emphasis given to the potential of interaction between anesthetics and other drugs which may be used in the project. All potential complications concerning anesthetics and related drugs as they affect research are not listed in this review. Our intent is to produce awareness that anesthetics may seriously alter pharmacological and physiological responses.

The following publications are excellent sources for additional information and were used extensively in compiling this review:

The Pharmacological Basis of Therapeutics (41)
Experimental Animal Anesthesiology (105)
Veterinary Anesthesia (69)
Textbook of Veterinary Anesthesia (122)
Comparative Anesthesia in Laboratory Animals (87)

History of Anesthesia (139)

The history of anesthesia dates back as early as the 15th century B.C. Sedatives and analgesics were extracted from plants by boiling in water. The Egyptians used opium and wines; the Chinese used hashish or wines containing hemp; and the Greeks used belladonna or opium in wine.

The use of analgesic drugs was common until the 16th through the 18th centuries, when their use for painful procedures was no longer taught or advocated. These were the centuries when witch hunting was in vogue and there was strong opposition to the use of magic potions. Drugs were replaced by hypnosis, refrigeration, and crushing the sensory nerves.

The first modern general anesthetic was nitrous oxide, discovered by Joseph Priestly in 1776. Dr. Crawford W. Long was the first to use ether clinically (1842). The barbiturates, discovered in the early 1900's, replaced ether and nitrous oxide for many surgical procedures. Newer inhalation agents such as methoxyflurane and halothane, which are safer and easier to control than the barbiturates, are now routinely used.

Ideally, an anesthetic agent should have a wide margin of safety, be a good analgesic, not depress the vital organs and the centers of the brain that control them, not need to be detoxified by organs such as the liver and kidneys, have a short induction and recovery time, and be nonexplosive. This ideal anesthetic agent has not yet been discovered. Research in analgesia and anesthesia is continuing in the search for the inhalation or injectable agent, or even such technics as acupuncture, that will meet the requirements of the ideal agent without deleterious side effects.

The exact mechanisms of action of the common anesthetic agents in use today are not known. Many theories have been proposed concerning the state of unconsciousness and narcosis (41A, 62, 122C, 139); however, none has met with general acceptance.

Anesthesia in Research - Complications

The researcher and laboratory animal veterinarian should be concerned with the role that anesthetics play in the interpretation of experimental results. Anesthetics may alter normal physiological and/or biochemical processes, not only during anesthesia, but also days or even weeks following anesthetic recovery. Complicating effects are numerous; and many changes that take place, especially at the biochemical and cellular levels, are just beginning to be investigated.

All anesthetic agents are not alike in their actions. If an anesthetic is required during an experimental procedure, the same agent and technic should be used throughout the experiment. While one anesthetic is liable to invoke a physiological change in one direction, another agent could produce the opposite effect.

Animal variations between species and even between strains may be responsible for individual animals behaving differently under the same anesthetic. Such factors as age, sex, weight, nutritional status, enzymes, strains within species, and circadian rhythms have been known to affect anesthetic response (87C).

The previous administration of anesthetics may alter the metabolism of subsequent compounds, as seen in rats pretreated with certain barbiturates. Drugs administered prior to or at the time of anesthesia may also influence the metabolism of anesthetics (87C). It is imperative that the investigator be familiar with the current literature regarding anesthetic interactions with other pharmacological agents. A review on pharmacology (98) describes a number of examples of how anesthetics may produce changes both by themselves or when combined with other pharmacological agents.

In any experiment in which an anesthetic, analgesic, or chemical restraint drug is used, proper controls must be employed to ascertain that the experimental results are not distorted by the drug. General anesthetics depress the cardiovascular and respiratory systems, resulting in altered blood gases, lowered metabolism, decreased body temperature, and alterations in perfusion.

Anesthesia is often a stressful experience resulting in endocrine changes. The various parameters such as blood gases, blood pressure,

cardiac output, body temperature, and any number of other factors that may contribute to interpretation of experimental results should be closely monitored and taken into consideration (87C).

Anesthetics may produce histopathologic changes in organs, which can be misinterpreted as being due to the experimental procedure. Examples are hepatic necrosis due to chloroform, and renal and hepatic lesions in the human due to methoxyflurane and halothane (87C).

Public Laws

PL 89-544, Laboratory Animal Welfare Act of 1966, as amended by PL 91-579, Animal Welfare Act of 1970, contains sections which directly pertain to the use of anesthesia in research work and the responsibility of the veterinarian and investigator:

Section 3.109 - Veterinary Care

In the case of a research facility, the program of adequate veterinary care shall include the appropriate use of anesthetic, analgesic, or tranquilizing drugs, when such use would be proper in the opinion of the attending veterinarian at the research facility. The use of these three classes of drugs shall be in accordance with the currently accepted veterinary medical practice as cited in appropriate professional journals or reference guides, which shall produce in the individual subject animal a high level of tranquilization, anesthesia, or analgesia consistent with the protocol or design of the experiment.

It shall be incumbent upon each research facility through its Animal Care Committee and/or attending veterinarian to provide guidelines and consultation to research personnel with respect to the type and amount of tranquilizers, anesthetics, or analgesics recommended as being appropriate for each species of animal used by that institution.

The use of these three classes of drugs shall effectively minimize the pain and discomfort of the animals while under experimentation.

Section 2.28 - Annual Report of Research Facilities

Each research facility shall submit on or before February 1, 1973, and on or before February 1 of each calendar year thereafter to the Veterinarian in Charge in the State where registered, an annual report signed by a legally responsible official covering the previous calendar year and showing that professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anesthetic, analgesic, and tranquilizing drugs, during experimentation, are being followed by the research facility during actual research or experimentation. Such report shall include: ....

c. The number of experiments conducted involving necessary pain or distress to the animals without the use of appropriate anesthetic, analgesic, or tranquilizing drugs and a brief statement explaining the reasons for the same: provided, however, that routine procedures (e.g., injections, tattooing, and blood sampling) do not need to be reported; and,

d. Certification by the attending veterinarian of the research facility or by an institutional committee of at least three members, one of whom is a Doctor of Veterinary Medicine, established for the purpose of evaluating the care, treatment, and use of all warmblooded animals held or used for research, or experimentations, that the type and amount of anesthetic, analgesic, and tranquilizing drugs used on animals during actual research or experimentation was appropriate to relieve all unnecessary pain and distress for the subject animals.

The National Institutes of Health issued a policy relating to laboratory animals which went into effect 1 July 1971 (NIH Guide for Grants and Contracts, No. 7, 14 Jun 1971). Animals used in activities supported by NIH must receive appropriate care and humane treatment. Grantees and contractors will:

a. Prove assurance of accreditation by a recognized professional laboratory animal accrediting body or of the establishment of a committee, at least one of whose membership is a Doctor of Veterinary Medicine, to evaluate the care of all warm-blooded animals held or used for research, teaching, or other activities supported by NIH grants, awards, or contracts; and,

b. Follow the guidelines prescribed in PHS Publication No. 1024, applicable portions of PL 89-544 as amended, the appended NIH Guidelines for Use of Experimental Animals, and the procedures described in this issuance.

The experiment should be so conducted as to avoid all unnecessary suffering and injury to the subject animals.

If the experiment is likely to cause greater discomfort than that attending anesthetization, the subject animals must first be rendered incapable of perceiving the pain and be maintained in that condition until the experiment is ended. The only exception to this guideline should be in those cases where anesthetization would defeat the purpose of the experiment, and then the procedures must be carefully supervised by the principal investigator.

The veterinarian should establish guidelines for the use of anesthetics, analgesics, and tranquilizers. All personnel using animals should consult with the veterinarian for guidelines regarding the above-mentioned drugs as well as the care and use of warmblooded animals.

Many anesthetics, narcotics, and tranquilizers are included in the Controlled Substances Act of 1970, PL 91-513. All personnel using these items should be familiar with this act and know the classification of

the drugs they are using and the appropriate recordkeeping, inventory, and security and control requirements.

Pain

The public laws and NIH guidelines place the responsibility on the veterinarian and investigator to recognize painful procedures and use appropriate drugs to effectively minimize the pain and discomfort of animals under experimentation (87B). It is not unusual for investigators to consider the pain perception of animals to be less intense than that of man and permit inhumane treatment of the animal on this basis.

Pain perception and reflex motor activity generally function in unison; however, in many instances reflex activity may not be an indicator of pain perception. Drugs such as curare and succinylcholine paralyze the animal and prevent reflex movement, and the animal, although unable to move, can perceive severe pain. Immobility, therefore, cannot be equated with a loss of the ability to perceive pain.

The perception of pain is a subjective response that occurs in the cerebral cortex and brainstem reticular formation, and depressing these two areas of the brain can alter pain perception. The status of pain in an animal can be monitored by observing the animal and physiological responses normally exhibited during a painful situation (87B). An animal in pain usually displays one or more of the following signs:

1. Attraction to the area of pain.
2. Increased skeletal muscle tone.
3. Altered electroencephalogram response.
4. Emotional response as demonstrated by increased blood pressure and heart rate, pupillary dilation, and a change in the respiratory pattern.

PREANESTHETIC PATIENT EVALUATION

Most laboratory animals are normal and healthy and can be identified as good anesthetic risks. Experimental animals at the USAF School of Aerospace Medicine (USAFSAM) are standardized before being issued to an investigator. Standardization at USAFSAM consists of a quarantine period of 30 days for quadrupeds and 60 days for nonhuman primates. The animals are treated for endoparasites and ectoparasites and are immunized for the appropriate diseases. An intradermal tuberculin test is administered to primates at 2-week intervals. All animals must be in good physical condition and have a complete blood count within normal limits before they are released from quarantine. Before an anesthetic is administered, a physical examination should be given, weight and temperature recorded, and a preanesthetic blood sample for a baseline complete blood count obtained.

When anesthesia is to be administered for surgery or to facilitate disease therapy in a sick animal, the risks of the anesthesia and the patient must be carefully assessed. Clinical laboratory tests evaluating renal, hepatic, and cardiovascular function, as well as fluid

and electrolyte balance and pH, may be necessary before appropriate care and anesthetics can be intelligently selected. The anesthetist should be aware of the pharmacological action of the drugs he is using and their relationship to the underlying disease. An example would be a male cat which has obstructive urolithiasis with secondary renal injury and uremia. An anesthetic may be needed to facilitate relieving the obstructed urethra; however, an agent such as a barbiturate or ketamine would be contraindicated since it must be excreted through the renal system. The anesthetist should be familiar with the anesthetic agents he routinely uses and know the permissible drugs and those to avoid for the commonly encountered clinical conditions (2).

The anesthetist should also be aware of indications for continuing or discontinuing drugs used to treat a medical problem prior to the administration of anesthesia (2).

Cortisone and related steroids--Continue administration. Prolonged administration causes hypofunction of the adrenal glands. Adrenal failure, characterized by hypotension, may result from the stress of surgery.

Phenothiazines--Discontinue the day before. An antinorepinephrine action hypotension which is unresponsive to therapy may result.

Rauwolfia alkaloids (reserpine)--Discontinue several weeks before. These drugs are antihypertensive and may produce hypotension by depleting serotonin and antagonizing norepinephrine.

Nonphenothiazine tranquilizers--Continue up to the time of the operation and resume afterward.

Narcotics and hypnotics--Use the same dose for premedication as the patient has been receiving.

Antihistamines--Continue use.

Antibiotics and Sulfonamides--Neomycin and kanamycin in large doses or if used with ether or muscle relaxants produce a neuromuscular blockade when given intravenously or intraperitoneally. Sulfonamides may produce methemoglobinemia and cyanosis.

Digitalis--Continue use.

Anticonvulsants--Continue use.

Cholinergic drugs--Discontinue 6 hours before anesthesia. May cause secretion of mucus, bronchospasm, or reflex cardiac effects.

Thiazide derivatives (diuretics)--Discontinue 4 days prior to anesthesia. Produces hypotensive action due to diminished pressor responses to epinephrine.

If possible, deficiencies such as anemia, dehydration, nephritis, and cardiac insufficiency should be corrected or compensated. Food and water are withheld 12-24 hours immediately before anesthesia to prevent regurgitation and subsequent inhalation pneumonia.

RESTRAINT

Laboratory animals come in a variety of sizes and dispositions. Before an anesthetic agent can be administered, adequate restraint, either physical and/or chemical, is necessary. Physical restraint of common laboratory animals is discussed and illustrated in an earlier aeromedical review (64). References on the restraint of large domestic animals (65), the laboratory dog (87H), and wild animals (69, 87K) are also available.

PREMEDICATION

There are three primary reasons to administer premedication before anesthesia:

1. Relieve apprehension and facilitate restraint.

2. Obtain an additive effect between depressant drugs of low analgesic or anesthetic potency.

3. Provide prophylaxis to prevent undesirable physiological effects of an anesthetic or surgical procedure; e.g.,

   a. Counteract hypotension.

   b. Decrease vagal effects.

   c. Reduce cardiac irritability.

   d. Decrease secretions.

   e. Decrease muscle tone.

Anticholinergics, tranquilizers, narcotics, and muscle relaxants are commonly used for preanesthetic medication.

Anticholinergics (41C, 69, 122)

The two most frequently used anticholinergics are atropine and scopolamine. They are belladonna alkaloids which compete with acetylcholine for the parasympathetic nerve endings, thereby preventing the transmission of impulses to the cholinergic effector organs. Scopolamine is the stronger blocking agent for the iris, ciliary body, salivary, bronchial, and sweat glands. Atropine has a more pronounced action on the heart, intestine, and bronchial musculature. They are rapidly absorbed from the gastrointestinal tract, mucous membranes, and to some extent from the skin. Most of these alkaloids are destroyed by enzymatic hydrolysis in the liver, but some are excreted unchanged by the kidney.

Advantages of anticholinergics as preanesthetics:

1. Decrease secretions from the mucous membranes and salivary glands.

2. Block vagal effects on the heart, thereby increasing heart rate.

3. Decrease tone and motility in the gastroinestinal tract.

4. Dilate the bronchus.

Possible complicating factors in research:

1. Electrical activity of the brain may be reduced with decreased alpha rhythm frequency, as seen in the electroencephalogram.

2. Intraocular pressure initially above normal is elevated further.

3. The rabbit has a high tolerance due to atropine esterase in the blood and liver.

4. Results may be complicated in learning and performance tests requiring memory and attention.

5. Normal cardiovascular physiologic responses may be altered.

Tranquilizers (41E, 69, 122)

Tranquilizers, which produce calmness of mind, have been classified by their chemical structure into four groups:

1. Phenothiazine derivatives.

2. Reserpine and related alkaloids.

3. Diphenylmethane derivatives.

4. Propanediol derivatives.

The phenothiazine group is most frequently used in veterinary medicine. These drugs depress the brain stem and its connections to the cerebral cortex and block autonomic ganglia. They also possess adrenolytic, antiacetylcholine, and antihistamine activity. They are generally not good analgesics.

Advantages of the phenothiazine tranquilizers as preanesthetics (69):

1. Decrease restraint required for refractory animals.

2. Potentiate anesthetics and analgesics, thereby resulting in smaller doses.

3. Prevent emesis.

4. Improve muscle relaxation.

5. Calm recovery from anesthesia.

6. Prevent epinephrine-induced ventricular fibrillation and vasoconstriction.

7. For hypothermia, disrupt hypothalamic temperature-regulating controls.

Possible complicating factors in research:

1. Psychology studies--results of learning and performance testing may be complicated.

2. Blood and bone marrow--agranulocytosis, aplastic anemia, pancytopenia, and other blood dyscrasias may occur.

3. Cardiovascular physiology--phenothiazines are alpha blockers but, individually, vary greatly in their adrenergic-blocking ability. They produce direct effects on the heart and blood vessels and indirect changes through the central nervous system and automatic reflexes. Vasodilatation, hypotension, and myocardial depression may occur. Hypotension can be reversed by norepinephrine; epinephrine is ineffective.

4. Body temperature--temperature-regulating mechanisms in the hypothalamus are disrupted.

5. Endocrine system--actions of many endocrine glands are altered due to the phenothiazine group's actions on the pituitary gland.

The following phenothiazine derivatives are used as preanesthetics (69):

Chlorpromazine HCl (Thorazine)--considered the prototype of the phenothiazine derivatives.

Promazine HCl (Sparine)--effects similar to chlorpromazine, with less hypnosis and fewer side effects.

Trifluprom azine HCl (Vetame)--comparable to promazine in its effects: 10 times the antiemetic effect of chlorpromazine and 3-5 times the tranquilizing potency.

Acetylpromazine Maleate (Acepromazine)--potent neuroleptic agent with low toxicity. It has been used in a wide variety of wild animal species.

Propiopromazine HCl (Tranvet)--more sedative and produces greater potentiation of barbiturates than chlorpromazine.

Methotrimeprazine HCl (Levoprome)--powerful nonaddictive analgesic sedative; 15 mg methotrimeprazine is equivalent to 10 mg morphine. A narcotics license is not required.

Xylazine (Rompun)--potent nonnarcotic sedative, analgesic, and muscle relaxant. A sleeplike state lasts 1-2 hours, while analgesia lasts 15-30 minutes.

Narcotics (41D, 69, 122)

Narcotics are the best parenteral analgesics available for use as an adjunct for surgical anesthesia and postoperative relief of pain. They (natural and synthetic) are controlled drugs and require strict security and records.

Narcotics produce marked analgesia, sedation hypnosis, euphoria, respiratory depression, nausea, emesis, and some peripheral vasodilation and hypotension. Morphine is conjugated in the liver and excreted in the urine.

Advantages of narcotics as preanesthetics (69):

1. The animal is quieted and more tractable.

2. Emesis and defecation are produced.

3. Anesthetic need is decreased.

4. Calm recovery from anesthesia is provided.

5. Postoperative pain is reduced and shock made less likely.

Possible complicating factors in research:

1. Respiration and blood pressure are depressed.

2. Morphine is unreliable in many species. Excitement may be produced in cattle, horses, swine, and cats.

3. The dog, rat, and mouse have a high tolerance and can degrade meperidine HCl (Demerol) more rapidly than man. These species should not be used if toxicology studies are to be correlated for the human.

4. Demerol should not be used on primates treated with isoniazid within 30 days; they may go into convulsions (107).

5. The heat-regulating mechanism of the hypothalamus may be altered.

Narcotic Agents--Morphine, Dilaudid, codeine, apomorphine, and heroin are derivatives of opium. Other narcotics, such as methadone and meperidine, are synthetic.

Morphine: the principal alkaloid of opium and one of the most effective analgesics.

Meperidine HCl (Demerol): analgesic effect is intermediate between codeine and morphine, without excitatory effects that morphine causes in many species. It significantly augments other sedatives.

Etorphine HCl (M-99): chemically related to morphine but more potent. Used primarily for restraint of wild animals.

Apomorphine: primary action is to stimulate the emetic center; emesis occurs within 3-10 minutes. This is a depressant and is contraindicated in the presence of previous central depression.

Fentanyl citrate-droperidol (Innovar-Vet): a combination narcotic-analgesic (fentanyl) and tranquilizer (droperidol) used to produce neuroleptanalgesia. It produces sufficient analgesia and sedation to permit minor surgical procedures. Fentanyl is 500 times more potent than meperidine. Analgesia, sedation, and respiratory depression are produced in 3-5 minutes. Droperidol produces sedation with decreased motor activity.

Pentazocine (Talwin): derived from a compound related to a narcotic antagonist (41D, 69, 111, 122). Pentazocine has approximately one-third to one-fourth the analgesic potency of morphine. Pentazocine is not classified as a narcotic and is not subject to narcotic controls since it is not addicting and may actually precipitate withdrawal symptoms in subjects physically dependent on morphine. It is absorbed well from the oral, IM, and subQ routes. Pentazocine is not routinely used as a preanesthetic because it is a poor sedative. It is primarily used for postsurgical analgesia. Naloxone HCl is the only narcotic antagonist that is effective for pentazocine.

Narcotic Antagonists (specific antagonists of narcotics)--

Levallorphan tartrate (Lorfan) and nalorphine HCl (Nalline): within 90 seconds following IV injection, almost all signs of morphine hypnosis disappear; 1 mg nalorphine is administered for each 10 mg morphine or 20 mg meperidine. When given without prior administration of a narcotic or in excessive doses, central nervous depression is produced.

Naloxone HCl (Narcan): 13 times more potent than nalorphine and 3 times more potent than levallorphan. Its chief advantage is that it does not produce the respiratory depression seen in other narcotic antagonists.

Cyprenorphine (M-285) and Diprenorphine (M-5050): potent antagonists used to reverse etorphine in wild animals. Because diprenorphine has very few side effects, it is replacing cyprenorphine.

Muscle Relaxants (41F, 69, 122J)

Depolarization and contraction of muscle fibers are initiated by the transmission of chemical mediators (acetylcholine) from presynaptic neurons to the motor end plates. Repolarization occurs when acetylcholine is removed from the synapse by the enzyme acetylcholinesterase.

The competitive neuromuscular blockers (d-tubocurarine chloride and gallamine) combine with the choline receptor sites and block acetylcholine. Ether, halothane, cyclopropane, streptomycin, neomycin, and polymyxin may have a synergistic effect on the competitive neuromuscular blockers. The dosage of ether and halothane should be halved when they are combined with muscle relaxants. Both d-tubocurarine and gallamine have a rapid onset (3-5 minutes) and are effective for 15 to 45 minutes. Antagonist to the curariform muscle relaxants are the

anticholinesterase drugs neostigmine (Prostigmine) and edrophonium (Tensilon). Neostigmine is administered at a rate of 0.03-0.10 mg/10 lb (4.5 kg) and may be supplemented in 5-8 minutes as needed at a dose rate of 0.015-0.005 mg/4.5 kg. Edrophonium is administered at a rate of 0.5-1.0 mg/4.5 kg and may be supplemented in 2-4 minutes at a dose rate of 0.25 mg/4.5 kg. Atropine 0.2 mg/lb (0.04 mg/kg) is administered with both neostigmine and edrophonium (69).

The depolarizing blockers (succinylcholine, decamethonium) produce depolarization at the neuromuscular junction. Patients exposed to cholinesterase inhibitors (found in certain insecticides) and anthelmintics (e.g., flea collars) have a more rapid and prolonged paralysis.

Muscle relaxants produce progressive paralysis which includes the respiratory muscles. These agents should not be used without adequate means of artificial ventilation. None of the muscle relaxants produce analgesia and should not be used for painful procedures without adequate anesthesia or analgesia. Advantages of muscle relaxants:

1. Relaxation during induction of anesthesia.

2. Relaxation for intubation in animals such as the miniature swine.

3. Supplement to spinal and regional anesthesia.

4. Apnea for thoracic surgery.

5. Muscle relaxation to facilitate surgical manipulations as in orthopedic surgery.

Gallamine and other neuromuscular blocking agents combined with local anesthesia have been used widely to produce long-term immobilization of experimental preparations for neurophysiologic and neuropharmacologic investigations. It has been learned, however, that the neuromuscular blocking agents produce significant changes in CNS excitability. Data from experiments in which these agents were used should probably be reevaluated. If neuromuscular blocking agents are to be used for studies involving the CNS, it is recommended that two or more immobilizing agents be tried serially to rule out the possibility of a central effect produced by the paralyzing agent (48).

INJECTABLE ANESTHETIC AGENTS

Barbiturates (41J, 69, 122)

The barbiturates are derivatives of barbituric acid. Hundreds of derivatives have been discovered; however, only a few are suitable for clinical use as anesthetics and sedatives. The barbiturates are divided into two classes, oxybarbiturates and thiobarbiturates. Structural changes which increase the fat solubility of the barbiturates increase the rapidity of onset and decrease the duration of action. The thiobarbiturates contain a sulphur radical which makes them highly fat soluble; therefore, their action is short lived.

The major barbiturates used in veterinary medicine are:

	Duration of Action
Phenobarbital Na (phenobarbitone)	long
Barbital Na (barbitone)	long
Amobarbital Na (Amytal)	intermediate
Pentobarbital Na (Nembutal)	short
Secobarbital Na (Seconal)	short
Thiopental Na (Pentothal)	ultrashort
Thiamylal Na (Surital)	ultrashort
Thialbarbitone Na (Kemithal)	ultrashort

Pentothal, Surital, and Kemithal are thiobarbiturates, and when administered intravenously in the dog their duration of action is approximately 1 hour. The period of surgical anesthesia is much shorter, approximately 15-20 minutes. Pentobarbital sodium has a duration of action of approximately 1-3 hours following IV administration in the dog. The thiobarbiturates and pentobarbital are the most popular barbiturates used in veterinary medicine, primarily because of their short duration of action compared to the other barbiturates.

The barbiturates are nonspecific depressants and exert their action on nervous, muscle, hepatic, and other tissues of the body. The central nervous system is very sensitive to the depressant action of these drugs; they would be of no clinical use if the CNS were not more sensitive than the other tissues.

The barbiturates are poor analgesics and muscle relaxants. Narcotics and/or nitrous oxide plus muscle relaxants are frequently used with the barbiturates to obtain adequate analgesia and relaxation. When analgesics and muscle relaxants are used, the barbiturate dosage may be halved. If more analgesia is needed during a surgical procedure, an analgesic should be given rather than more barbiturate.

The barbiturates are readily absorbed and have been administered by a number of routes--intravenous, oral, intramuscular, intraperitoneal, and intrathoracic. The onset and depth of anesthesia is difficult to control by any route other than intravenous. The other routes are used due to ease of administration, especially in wild animals or small laboratory animals such as rodents where it is difficult to perform a venipuncture. The inhalation anesthetics and some newer injectable anesthetics have a wider margin of safety than the barbiturates and should be used in those animals where it is not feasible to administer drugs IV.

The barbiturates are very alkaline (pH near 11) and are irritating to tissues. When barbiturates are injected outside of a vein, they can produce tissue necrosis and sloughs. These sloughs can usually be prevented by infiltrating the tissues with a local anesthetic to produce vasodilatation, which aids diffusion and neutralizes the alkaline pH,

or by infiltrating the tissues with saline to dilute the barbiturate. Corticosteroids may be used to reduce the inflammatory response.

The long-acting barbiturates such as phenobarbital and barbital are not metabolized by the liver and are excreted unchanged by the kidneys. The intermediate and short-acting oxybarbiturates are transformed in the liver, whereas the ultrashort-acting thiobarbiturates are metabolized by the liver as well as other tissues (kidney, brain). Hepatic or renal disease can result in toxic accumulation of the barbiturates, with resultant coma and death.

All barbiturates possess approximately the same margin of safety. The anesthetic dose is approximately 50%-70% of the minimum lethal dose. Death is usually the result of respiratory failure due to depression of the respiratory centers. The heart usually continues to beat until it becomes hypoxic. With adequate artificial ventilation, many barbiturate deaths can be prevented.

The barbiturates, due to their general depressant characteristics, produce the following changes:

Respiratory. All respiratory driving forces are depressed (pneumotaxic, CO_2 and pH, and hypoxic). Adequate management of ventilation is required to prevent respiratory acidosis and eventual metabolic acidosis.

Cardiovascular. The vasomotor center and the heart are depressed by the barbiturates. Cardiac output decreases, peripheral resistance increases, and heart rate may increase or remain stable. Variable changes occur in blood pressure.

Renal. Urine production decreases as a result of hypotension (prerenal uremia) and direct depression of tubular cells. Renal depression may result in uremia and decreased excretion of the barbiturates, thus prolonging anesthesia.

Hepatic. Inadequate circulation to the liver will delay hepatic metabolism of the barbiturates. Hypothermia, acidosis, low oxygen tension, and hypotension, which can occur during barbiturate anesthesia, all contribute to reduced hepatic function.

Central nervous system. The CNS, neuromuscular junctions, and autonomic ganglia are depressed.

Uterine. Anesthetic doses depress uterine contraction and cross the placental membrane to depress the fetus.

Barbiturates are potent enzyme inducers and may influence the metabolism of subsequently administered drugs (23).

Urethan (Urethane, Ethyl Carbamate)

The urethanes are feeble and toxic hypnotics (41J) and have been used primarily in laboratory animals and fish. In large doses they produce bone marrow depression, and they are hepatotoxic. The urethanes are carcinogenic in mice, rats, rabbits, and are therefore a potential hazard (5, 143).

Chloral Derivatives

Chloral hydrate and trichloroethanol are halogenated ethanols. The CNS depression produced by chloral hydrate is believed to be due to trichloroethanol to which chloral hydrate is rapidly reduced (41J). Chloral hydrate is a poor analgesic. The respiratory and vasomotor centers are severely depressed. It has a low margin of safety and is not a satisfactory anesthetic (69).

Chloralose (alpha-D-glucochloralose, Chloralosane) produces light anesthesia lasting for several hours. It has been used primarily in studying cardiovascular physiology because it depresses motor and sensory spinal centers without interfering with respiratory and cardio-reflexes (54). Respiration is not depressed. Tachycardia is usually present and blood pressure is normal or increased. Its main disadvantage is its insolubility.

Dissociative Agents

This relatively new group of drugs are termed dissociative agents because they selectively interrupt association pathways to the brain before blocking proprioceptive and tactile sensation. Their effects are dose dependent; low doses produce immobilization, and high doses provide analgesia and anesthesia. Unconsciousness is characterized by catalepsy (loss of voluntary motion, muscle rigidity with the muscles remaining in a fixed position, eyes open, and many reflexes remaining intact). The dissociative agents, in contrast to the paralyzing agents, provide good analgesia and amnesia at anesthetic dosage. There is tremendous species variation for these agents. Many species are stimulated to the point of clonic convulsions, rather than being depressed. In species that can safely receive these agents, they provide excellent restraint and analgesia-anesthesia with a wide margin of safety and minimal respiratory or cardiovascular depression. The following dissociative agents are currently being used clinically or experimentally:

Phencyclidine (Sernylan, Sernyl, CI-395) (20, 42, 85, 105F)--Phencyclidine is recommended for use in nonhuman primates only. It is administered by the intramuscular route. There is a species variation in the primates for onset and duration of effects. The onset ranges from 5 to 30 minutes, and duration of action can be from 15 minutes to several hours. In the nonhuman primate, low doses produce calmness; as the dose is increased, analgesia, catalepsy, and anesthesia are produced. Muscle relaxation is poor.

When used in conjunction with the barbiturates, there is a synergistic effect. The ultrashort-acting barbiturates should be used to achieve precise titration. Respiratory depression does not occur when phencyclidine is used by itself; however, severe depression may occur when it is used with the barbiturates.

Undesirable side effects are salivation, disorientation, hypothermia, and mild excitement to convulsions and hallucinations during recovery. Hyperactivity is observed in rats and mice. Low dosage produces a calming effect in the pigeon, guinea pig, hamster, rabbit, cat, dog, and monkey. Convulsive seizures occur in the pigeon, guinea

pig, dog, and monkey at doses higher than required for general anesthetic. For species such as the dog, there is a narrow margin between the anesthetic and convulsive dose. Phencyclidine is not used in human anesthesiology because of the incidence of psychotic behavior that follows its use.

Ketamine (Vetalar, Ketalar, CI-581) (42, 70)--Ketamine is a derivative of phencyclidine with one-sixth its potency. Ketamine is approved for use in felines, nonhuman primates, and humans. It can be administered by the intramuscular or intravenous routes. Ketalar is the human product, and Vetalar is the veterinary counterpart. It has a wide margin of safety with less side effects than phencyclidine. Anesthesia is characterized by rapid onset, profound analgesia, minimal respiratory depression, slight cardiac stimulation, and intact laryngeal and pharyngeal reflexes. Ketamine is detoxified and excreted by the liver. At anesthetic doses, the duration of action is approximately 30 minutes. Undesirable side effects are similar to those described for phencyclidine. Myoclonic jerking or tonic convulsions are not dose dependent and occur in 2%-5% of the cases. They can be controlled by ultrashort barbiturates or phenothiazine tranquilizers.

Tiletamine CI-634) (42)--Tiletamine is a new product being used on a trial basis and is not on the commercial market. It is one-half as potent as phencyclidine and three times as potent as ketamine. It may be administered by the intramuscular, intravenous, or subcutaneous routes. Pharmacologically it behaves like ketamine. Anesthesia and analgesia are sufficient for minor surgical procedures. Tiletamine possesses a wide margin of safety for a number of different species, and is effective in primates, felines, carnivores, ruminants, and birds. Induction is quiet, and recovery occurs within 1 hour. It is noncumulative in action when administered repeatedly. It crosses the placental barrier but is rapidly metabolized by the neonate. Undesirable side effects are similar to those of phencyclidine and ketamine.

CI-744 (14, 42)--This is an unnamed combination of tiletamine (CI-634) and a tranquilizer (CI-716). CI-634 and CI-716 are synergistic and, together, provide an excellent anesthetic without the many undesirable side effects of dissociative agents when used alone. CI-744 provides rapid immobilization with a wide margin of safety in many wild and domestic animals. Unlike phencyclidine and ketamine, it can be used in the dog. Anesthesia with good muscle relaxation is satisfactory for major surgery. The anesthetic time is dose dependent.

INHALATION ANESTHESIA

Inhalation anesthetics provide the safest type of anesthesia if they are properly administered. The anesthetic level can be easily controlled. If ventilation and circulation are adequate, the anesthetist can increase or decrease the degree of anesthesia rapidly by varying the amount of anesthetic delivered to the lung. Insignificant amounts of inhalant anesthetic are biodegraded; therefore, detoxification is not dependent on the liver and kidneys.

Although the inhalant anesthetics are safe, they are the most complex to administer, requiring a trained anesthetist and often

sophisticated and expensive equipment. If the inhalant anesthetics are not administered properly, they may possess a narrow margin of safety. Some agents also have the disadvantage of being explosive or able to support combustion, irritating to the respiratory system, and possibly a factor in producing hepatic or renal pathology.

The depth of general anesthesia varies directly with the partial pressure of the anesthetic in the brain tissue, which approximates the anesthetic level in arterial blood. Several factors influence the arterial and brain anesthetic level (41L):

1. Concentration of anesthetic.
2. Pulmonary ventilation.
3. Transfer of anesthetic from alveoli to circulating blood.
4. Loss of anesthetic from the arterial blood to the body tissues.

These factors are divided into three phases of anesthetic distribution--pulmonary, circulatory, and tissue (41L):

Pulmonary Phase

Respiratory Rate and Tidal Volume--These directly affect the volume of anesthetic gases and vapors delivered to the alveoli.

Vaporization--The ease with which volatile anesthetics vaporize depends on their physical properties. The concentration of vapor that can be delivered by a saturation vaporization at room temperature varies with the vapor pressure of the volatile anesthetic.

Anesthetic	Vapor pressure @ 20°C (mmHg)	Concentration of vapor @ 20°C (%)	Induction (%)	Maintenance (%)
Ether	443	58	10-40	5-15
Halothane	243	32	1-4	0.5-2
Chloroform	160	21	0.5-1.5	0.25-1
Methoxyflurane	24	3	3-4	0.25-1

Ether and halothane vaporize readily at room temperature. Gases at sea level produce a total of 760 mmHg pressure. Ether when fully vaporized composes 443 mmHg, or 58% of the total gas volume (443/760). Methoxyflurane vaporizes very poorly at room temperature and, when fully saturated, makes up only 3% of the gas volume delivered to the patient. Halothane is a potent anesthetic requiring only 1%-4% concentration for induction; however, since it produces a 32% concentration at 20°C, it requires a sophisticated vaporizer with accurate controls to prevent an overdosage. The safety in methoxyflurane lies in its low vapor pressure. At room temperature it is almost impossible to produce a concentration that will result in overdosage; however, if the temperature in the vaporizer is raised above 20°C, an increased vapor concentration and overdosage will be produced.

Concentration Effect (31)--During anesthetic induction, the concentration of anesthetic is high in the alveoli compared to in the

pulmonary blood. The anesthetic diffuses rapidly from the alveoli to the blood until an equilibrium is approached. A high concentration of anesthetic must replace that lost to the pulmonary blood to maintain the gradient. Induction concentration and flow are initially high (4% halothane) and then reduced to a maintenance level (0.25%-2% halothane) once the alveolar and blood concentrations are equilibrated.

Diffusion Hypoxia (33)--Diffusion hypoxia is the reverse of the concentration effect and occurs during recovery when there is a high level of nitrous oxide in the blood and the patient is taken off of all gases and oxygen. The gradient is reversed and the nitrous oxide enters the alveoli in an attempt to produce an equilibrium; as a result, there is little space for air to enter during inspiration. For this reason, 100% oxygen should be given for 3-5 minutes after taking the patient off of high levels of nitrous oxide.

Second-Gas Effect (32)--The uptake of 1% halothane is more rapid when administered with 70% N_2O than with 10% N_2O. Because of the concentration effect, 70% N_2O diffuses more rapidly from the alveoli into the blood than does the 10% concentration. The ability of one gas to influence the uptake of a second gas because of the concentration effect is known as the second-gas effect.

Circulatory Phase

The gases diffuse across the alveolar and capillary epithelium and are dissolved in the pulmonary capillary circulation and transported to the body tissues. The uptake of gases into the blood depends on the solubility of the gas in blood and the rate at which the anesthetic is transported from the lungs (cardiac output).

Some tissues are preferentially supplied by blood and therefore are affected more rapidly by the anesthetic. The brain is 2.2% of the body weight and receives 14% of the cardiac output; therefore, a large percentage of the anesthetic rapidly diffuses into the brain. Hypercarbia due to poor ventilation or inadequate CO_2 reabsorption in a closed system increases cerebral blood flow and, thus, anesthetic delivery to the brain.

Tissue Phase

The anesthetic diffuses from the circulation into both nervous and nonnervous tissues. A stable cerebral anesthetic concentration is desired and requires equilibration with the concentration in the nonnervous body tissues.

The blood and tissues of the body act as a reservoir or sponge to absorb the anesthetic agent (105E). When the tissues and blood are saturated with the anesthetic, the partial pressure of the gas in arterial blood will increase significantly, resulting in increased concentrations of anesthetic being delivered to the brain. During induction, gases which are very soluble are easily absorbed into blood and tissues--which act as a buffer and prevent a rapid increase in arterial partial pressure of the gas. During recovery, the large quantity of

soluble anesthetics stored in the body tissues are released slowly from these tissues, maintaining an elevated arterial concentration and prolonging recovery from anesthesia. Insoluble anesthetic gases are not readily dissolved in blood and tissues; therefore, the blood partial pressure can be rapidly increased or decreased by controlling the alveolar concentration, with resultant rapid induction and recovery. Order of solubility:

1. Diethyl ether--most soluble, slow induction, slow recovery.
2. Methoxyflurane (Penthrane, Metofane).
3. Chloroform.
4. Halothane (Fluothane).
5. Nitrous oxide.
6. Cyclopropane--least soluble, quick induction, quick recovery.

Most anesthetic agents have similar blood and tissue solubility coefficients. Halothane, however, is over twice as soluble in brain tissue as in blood and is therefore rapidly absorbed into the brain.

Diffusion of anesthetic from one tissue to another may be significant. A reequilibration of anesthetic may occur where there is a sudden alteration of fluids, as seen in cardiopulmonary bypass, excessive dermocysis, and peritoneal lavage.

VOLATILE ANESTHETICS

The volatile anesthetics are extremely potent and relatively soluble in blood and tissues. Chemically the volatile anesthetics are divided into the ethers and halogenated hydrocarbons.

Halothane (Fluothane) (41I, 122)

Chemical Properties--Halothane interacts with rubber and some plastics; therefore, the vaporizer is usually drained between uses and the rubber hoses washed out. It might cause the plastic valves in the anesthetic machine to stick, so the valves should always be checked before surgery.

General Anesthetic Action--Halothane is a poor analgesic, recommended only in combination with N_2O. It is also potent and should only be used with an accurate out-of-circle vaporizer. Halothane produces poor muscle relaxation. Inhalant induction is fairly rapid in combination with N_2O (1%-4% for induction and 0.5%-1% for maintenance).

1. Cardiovascular effects. Blood pressure, myocardial contractile force, cardiac output, and total peripheral resistance (i.e., peripheral vasodilatation) are reduced. The heart rate slows with deep anesthesia and is an indication of depth of anesthesia. The myocardium is sensitized to catecholamines, and arrhythmias may occur. Bradycardia is usually alleviated with atropine.

2. Liver. Centrolobular necrosis has been observed in a small percentage of humans 5 days to 3 weeks following halothane anesthesia. A cause-effect relationship has not been established.

3. Respiratory effects. Tidal volume is decreased while heart rate increases slightly. Halothane inhibits laryngospasm and coughing but produces bronchial dilation.

4. Gastrointestinal effects. Motility is depressed.

5. Uterus. Contraction is inhibited.

Halothane is popular for balanced anesthesia. There is a small margin between anesthesia and toxicity, but this danger is lessened by sophisticated vaporizers and N_2O--which reduces the halothane dosage by one-half to two-thirds. It is not recommended for small laboratory animals. Depth of anesthesia can be altered rapidly and careful monitoring is mandatory. Halothane, especially in combination with succinylcholine, has been implicated in the production of malignant hyperthermia (hyperpyrexia) in man and some strains of minipigs.

Methoxyflurane (Metofane, Penthrane) (41I, 122)

Chemical Properties--Methoxyflurane is a clear, colorless liquid with a fruity odor. The low vapor pressure at room temperature is barely sufficient to induce anesthesia.

General Anesthetic Action--Veterinarians generally consider this a complete anesthetic because of its good analgesia and muscle relaxation. Human anesthetists routinely supplement methoxyflurane with N_2O and muscle relaxants. Inhalant induction and recovery are slow, with odor persisting on the breath for several days. It can be vaporized with an in-circle wick vaporizer. The maximum concentration that can be attained at room temperature is 3%-4% for induction (0.25%-1% for maintenance).

1. Cardiovascular effects. Effects are similar to those of halothane, but to a lesser degree. There may be some hypotension due to reduced cardiac output. Sinus bradycardia may occur and can be reversed with atropine. Essentially no arrhythmia occurs.

2. Respiratory effects. Respiratory depression is marked; therefore, an endotracheal tube should always be used. Vaporizing to lethal concentrations is considered difficult, but this can occur if intentionally hyperventilated.

3. Uterus. Contractility is not affected.

4. Gastrointestinal effects. Nausea and vomition occasionally occur.

The low vaporization pressure and complete anesthesia make methoxyflurane ideal for the less experienced anesthetist. It does not require expensive equipment and can be used for small laboratory animals. Its main disadvantage is the nausea and vomiting it produces. Methoxyflurane has been implicated as a cause of hepatic damage.

Diethyl Ether (Ether) (41I, 122)

Chemical Properties--Ether is a colorless, highly volatile liquid which has a pungent odor and irritating vapor. It is marketed in metal containers lined with copper to retard oxidation. Ether and air slowly form ether peroxides which react with alcohol to form acetaldehyde. These compounds are unstable and are flammable and explosive.

General Anesthetic Action--Ether is a potent and complete anesthetic. The analgesia and muscle relaxation are exceptionally good. Inhalant induction is slow and difficult (10%-40% for induction, 5%-15% for maintenance).

1. Analgesia. Even at subanesthetic levels, analgesia is excellent.

2. Cardiovascular effects. Myocardial contractility is significantly depressed; however, the sympathetic stimulation ether produces usually results in a normal cardiac output and blood pressure. Heart rate is frequently increased. Normal blood pressure may be maintained in Stage III, planes 1 and 2; but at a deeper level, the blood pressure decreases. During induction there may be atrioventricular nodal rhythm disturbances against which atropine is not effective. At light levels there is peripheral vasodilatation.

3. Respiratory effects. Ether is irritating to the respiratory passages and stimulates bronchial secretions. The secretions can be blocked with atropine or scopolamine. Respiratory rate and tidal volume are increased even in deep anesthesia. It is generally considered contraindicated in any respiratory impairment.

4. Gastrointestinal effects. Nausea and vomiting occur.

5. Genitourinary effects. Urine production is decreased with renal vasoconstriction, decreased glomerular filtration, and tubular water reabsorption. Uterine activity is only slightly affected by ether.

6. Liver. Hyperglycemia and metabolic acidosis frequently occur in the dog.

7. Body distribution. Induction is so slow that 20 hours is required before 90% of inspired tension is reached in arterial blood (very soluble in tissues); also, ether requires several hours to leave the body tissues.

Ether is a versatile anesthetic, but its flammability and mucosal irritation have decreased its use. It is currently only used in pediatrics where spontaneous respiration is encouraged or when good anesthetic equipment is not available.

Chloroform (41I)

Chemical Properties--Chloroform is a sweet-smelling liquid. It is marketed in a brown bottle to retard decomposition and oxidizes to irritating phosgene.

General Anesthetic Action--It once enjoyed wide use, particularly in obstetrics. An accurate vaporizer is required for good control; however, such vaporizers were not available during the time of its popularity. Historically, death occurred early in anesthesia; excited patients with high catecholamine levels would go into ventricular fibrillation when chloroform was given.

1. Respiratory effects. Rate increases and tidal volume decreases; respiration is rapid and shallow.

2. Cardiovascular effects. Myocardial contractility, cardiac output, vascular smooth muscle contractility, and blood pressure decrease. Arrhythmias occur. The myocardium is sensitized to catecholamines. Bradycardia and hypotension are danger signs.

3. Liver. Central lobular necrosis and fatty degeneration frequently cause clinical problems.

Effects of chloroform are similar to those of halothane, but bad reputation of toxicity has caused its discontinued use. It is contraindicated in cardiac, renal, or hepatic disease.

ANESTHETIC GASES

Anesthetic gases are chemicals that are generally present as gases at room temperature and must be stored in cylinders under pressure.

Nitrous Oxide (N_2O) (41H)

Chemical Properties--It is a colorless gas with a sweet odor and is marketed in steel cylinders as a colorless liquid under pressure. It is nonexplosive and nonflammable, but will support combustion. It is the only inorganic gas that is practical for clinical anesthesia.

General Anesthetic Action--Its anesthetic action is weak and it cannot produce surgical anesthesia by itself. The agent is most useful at 35%-50% when combined with halothane. Care must be taken that the inspired gas mixture contains at least 20% oxygen.

1. Analgesia. It produces excellent analgesia and is frequently used by itself in humans to decrease pain, without decreasing uterine contraction, during the second stage of labor.

2. Cardiovascular effects. Effects are negligible; 80% N_2O slightly depresses myocardial contractility and slightly increases the response to norepinephrine.

3. Respiratory effects. Effects are negligible; 50% N_2O slightly elevates the resting minute volume without affecting the CO_2 response.

4. Gastrointestinal, neuromuscular, liver, kidney, and hematopoiesis. Effects are negligible.

N_2O is excellent for basal anesthesia and analgesia if combined with other drugs. If hypoxia is avoided (i.e., diffusion hypoxia), it is essentially innocuous.

Cyclopropane (trimethylene)(41H)

Chemical Properties--It is a colorless gas with a characteristic odor and is stored in metal cylinders as a liquid under pressure. It is heavier than air, flammable, and explosive.

General Anesthetic Action--It is the most potent of the commonly used anesthetic gases and is an excellent analgesic. There is a wide margin of safety. It should be used in a closed-circle system to prevent explosive concentrations in the room air.

1. Cardiovascular effects. Except for its effects on cardiac rhythm, effects are relatively benign. The myocardium is sensitized to catecholamines. Many arrhythmias, especially A-V nodal rhythm and premature ventricular contractions, are produced. Generally, there is an increased sympathetic tone with a slightly increased cardiac output and peripheral resistance. Blood pressure is slightly elevated. Heart rate is normal or somewhat slow.

2. Respiratory effects. No stimulation during induction, and slightly decreased ventilation during surgical anesthesia.

3. Liver. There is a transient reduction in function as determined by BSP and glucose tolerance.

4. PVCs. There is an increase as a result of plasma volume decrease.

5. Gastrointestinal effects. Tone increases.

Because of its potency and controllability, cyclopropane is a popular anesthetic despite its explosiveness. It is frequently used in poor-risk patients with cardiac disease. The addition of curariform muscle relaxants can reduce the required anesthetic concentration and, therefore, significantly reduce the danger of arrhythmia. In human hospitals, only an anesthesiologist may administer cyclopropane.

ENDOTRACHEAL INTUBATION

All animals under anesthesia should be intubated. This procedure is necessary for efficient administration of inhalant anesthetics and for thoracic surgery; it also enables unrestricted ventilation when noninhalant anesthetics are administered. Secretions or vomitus are prevented from entering the trachea, especially when the animal has lost its swallowing reflexes. The endotracheal tube should be left in the patient following anesthesia until the swallowing reflexes have returned. Care must be taken that the patient does not chew the tube and possibly inhale portions into the bronchus.

Endotracheal catheters are available in many sizes and varieties, and a wide array should be purchased. A set containing the following would be a minimum for preparation of all sized patients.

14 French - I.D. 3.5 mm	30 French - I.D. 7.8 mm
28 French - I.D. 6.5 mm	36 French - I.D. 8.5 mm

The largest diameter endotracheal tube that will easily fit into the trachea should be selected. The anesthetist should take care not to insert the tracheal tube too far down the trachea, to prevent the tip from entering one mainstem bronchus while occluding the other bronchus.

A clear plastic tube is preferred so that materials (fluids, blood) inside may be visualized. Unclean tubes are a source of infection. All tubes should have an operational cuff. Failure to have a good cuff or to use the correct size tube may allow leaks around the tube and result in failure to achieve the desired depth of anesthesia.

Technics

Tracheal tubes may be placed through the larynx with the aid of a laryngoscope or tissue forceps, or passed blindly using the fingers of one hand to guide it into the larynx. The tubes are generally placed through the oral pharynx into the trachea (Fig. 1), but smaller ones may be passed through the nose, especially for oral surgery.

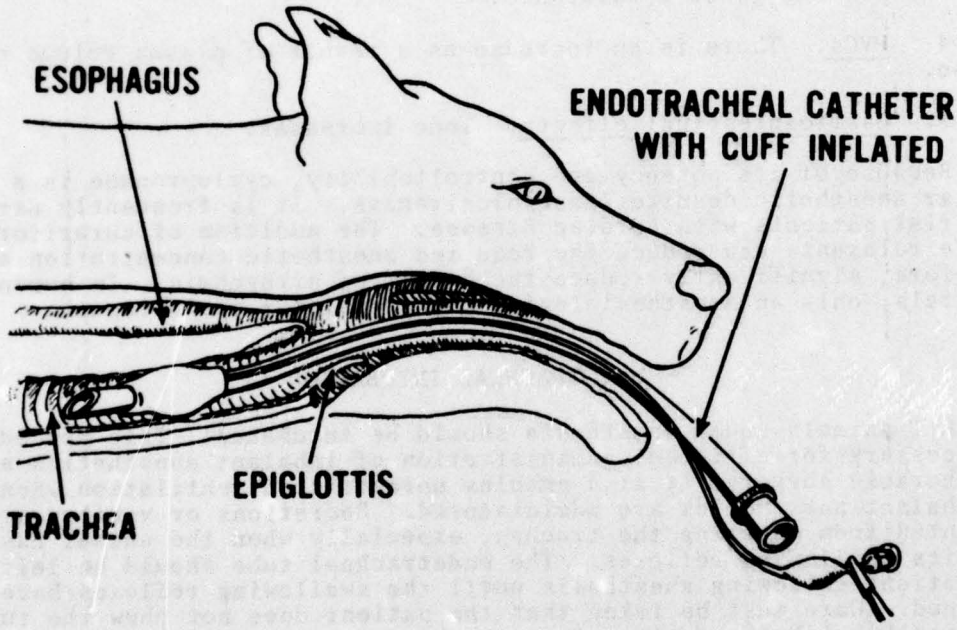

Figure 1. Endotracheal catheter with inflatable cuff in position.

It is easier and safer to intubate after the laryngeal reflexes have been rendered inactive by anesthesia--barbiturates administered intravenously or gas anesthesia administered by a face mask. It is advisable to spray the laryngeal area with a local anesthetic to reduce

laryngospasm, especially in cats and primates. The tracheal tube should be lubricated with an agent such as K-Y jelly, or at least moistened with water. After the tube is inserted, there may be some coughing from its physical presence in the trachea. Atropine should be administered prior to intubation to help prevent vagal stimulation and reflex bradycardia.

A strip of moistened gauze is tied around the tracheal tube and then tied around the maxilla unless this area is in the surgical field, in which case the tube can be tied to the mandible. In primates, the tube may be sutured to the lips with a single stitch.

Miniature swine are difficult to intubate because of their laryngeal anatomy and the long distance from the snout to the larynx. To enable visualization of the arytenoid cartilages, the pig is placed in sternal recumbency. Two technicians hold the pig's mouth open with gauze strips and retract the tongue. A portable surgery lamp is directed over the shoulder of the person intubating the pig so that the epiglottis and arytenoid cartilages may be seen. A sponge forcep holding a 4x4-in (10- x 10-cm) gauze sponge is used to clear the pharynx of secretions and then to grasp and retract the epiglottis. A slightly curved wire stylet is inserted into the endotracheal tube. The curve of the tube is directed dorsally into the larynx and then rotated ventrally into the trachea to bypass the middle laryngeal ventricles. Whereas a large dog can be intubated with a 40 French tube, miniature swine weighing 30 to 60 kg often cannot be intubated with a tube larger than 32 French. The key to successful intubation of the pig is adequate visualization of the arytenoid cartilages, with the pig sedated sufficiently to prevent laryngeal spasm when a tube is passed. *Benzocaine* (Cetacaine) may be sprayed topically to help control laryngospasm during intubation.

Complications

With intubation, complications due to animal physiology or to handling technic can occur. Some of these are seen in Figure 2.

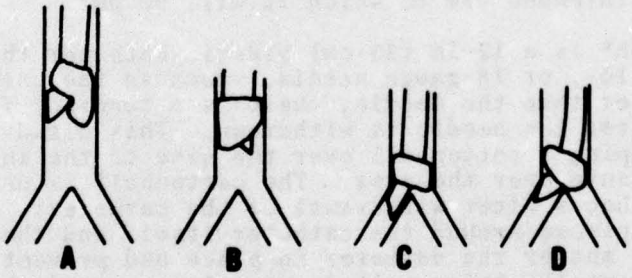

Figure 2. Complications of endotracheal intubation: A--Asymmetrical balloon; B--Balloon too close to end of tube; C--One bronchus occluded; D--Both bronchi occluded.

An asymmetrical balloon can force the end of the tube against the wall of the trachea, causing the tube to be occluded. If placed too close to the end of the tube, a balloon that is overinflated will expand over the end of the tube and reduce gas flow. Overinflation of

the cuff can traumatize the trachea and obstruct blood flow, resulting in pressure necrosis. If the tube is jammed into one mainstem bronchus, the balloon can block one lung; if the end of the tube is occluded, both lungs can be blocked.

Internally, a soft tube may double in the trachea and become crimped. Externally, a tube may be bent over the teeth or at its end near the connector. A right-angle (90°) connector can prevent this type of crimping. A recovering patient should be observed frequently; upon awakening, the patient may bite down on the tube and occlude it.

Laryngeal edema may occur; the cat and primates are especially susceptible. If edema does occur, it may be treated with steroids and diuretics; but the best "treatment" is a prophylactic (gentle) intubation technique.

Bradycardia and arrhythmias have been reported because of increased vagal tone during insertion of the tube. Preanesthetic use of atropine will prevent vagal stimulation.

Laryngospasm can be reversed by intravenous atropine. Topical anesthetics applied to the larynx may help prevent laryngospasm.

INJECTABLE ANESTHETIC TECHNICS

Intravenous Route (82G, 122G)

The area for venipuncture is shaved, cleansed, and disinfected. A tourniquet is applied or an assistant's hand is used to immobilize the vein and prevent venous drainage, thereby causing the vein to distend. The needle is introduced through the skin and into the vessel with the bevel up, and should be threaded up the vein. Intravenous catheters are easy to use and eliminate the possibility of perivascular injections. Two types of intravenous catheters are in general use. The type selected will depend partially on personal preference and partially on the intended use to which it will be put.

The Intracath* is a 12-in (30-cm) plastic catheter that fits inside of a 14-, 16-, or 18-gauge needle. Because the catheter is smaller in diameter than the needle, there is a tendency for blood to leak around it after the needle is withdrawn. This disadvantage can be overcome by taping a cottonball over the site of the insertion to apply slight pressure over the area. The cottonball is usually left in place several hours after withdrawal of the catheter. A second piece of tape is placed around the catheter itself and then passed around the leg to anchor the catheter in place and prevent it from slipping or accidentally being pulled out. Tape around the needle guard will not anchor the catheter because the catheter will slip freely through the needle. Paper masking tape works well for this purpose since it does not stick to hair very well and is easy to remove. Removal of the tape is also facilitated if the free end is turned under against itself to form a small tab.

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*C. R. Bard, Inc., Murray Hill, N.J.

Because of its length, the Intracath may be used in the jugular vein even in large dogs to measure central venous pressure (CVP). It may also be used in an exteriorized carotid artery (carotid loop) to sample arterial blood and measure pressure in the aortic arch or proximal descending aorta, or it may be passed percutaneously into the femoral artery and advanced into the terminal descending aorta for the same purpose.

Intravenous catheters of the Jelco* or Longdwell** type fit over the outside of the needle. Since these catheters are larger in diameter than the needle, they are less likely to leak blood around the catheter. Although the end of the catheter is beveled down to the needle, it may be difficult to insert. It helps to slightly nick the skin with a scalpel at the site of insertion. These catheters may be used to record blood pressure, collect blood samples, or inject irritating solutions; however, since they are only 2-2.25 in (5-6 cm) long, they are too short to be used for recording the CVP.

Whether making a single IV injection or introducing an IV catheter for serial or continuous injections, certain veins are easily accessible. The same veins are not prominent in all species; some veins that may be used in certain species are listed below:

Dog

Cephalic vein

Recurrent tarsal vein

Jugular vein

Sublingual vein (requires a small-gauge needle (26-27 gauge). A sublingual hematoma may develop but can usually be controlled with pressure.

Cat

Cephalic vein

Great saphenous vein (medial side of hind leg)

Jugular vein

Primate (such as rhesus and cebus)

Popliteal vein (posterior surface of "calf" of leg)

Pigs and rabbits

Marginal ear vein (on posterior or lateral edge of ear--not the center vessel which is an artery)

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* Jelco Laboratories, Raritan, N.J.
** Becton, Dickinson & Co., Rutherford, N.J.

Large animals (such as horse, cow, sheep, goat)

Jugular vein

The barbiturates are routinely administered by the intravenous route. One half of the calculated dose is injected rapidly (5 to 10 seconds) so that the animal passes fairly quickly through the excitatory stage into light surgical anesthesia. The second half of the dose is titrated slowly over a period of 5-10 minutes until the desired depth of anesthesia is achieved. For the barbiturates, the IV route is best since the desired anesthetic level is achieved rapidly and the depth of anesthesia is easy to titrate. In small animals a low-concentration anesthetic should be used to prevent accidental overdosage. Commercially prepared solutions may be diluted with sterile water before injecting. When a sedative preanesthetic such as a narcotic or tranquilizer is used, the calculated dose of the injectable anesthetic should be halved.

Apnea sometimes occurs when the barbiturate anesthetics are administered too rapidly. The larynx should be stimulated or the chest compressed to initiate the respiratory reflexes and breathing. If breathing does not resume, an endotracheal tube should be inserted at once and the animal ventilated. Failure to do so usually leads to cardiac arrest and death.

The patient should be weighed on accurate scales immediately prior to being anesthetized so that the correct dosage can be calculated for an injectable anesthetic. The solution should be prepared to the desired concentration and accurately labeled with the date it was prepared and the concentration. The percent solution of a liquid anesthetic is calculated by the number of grams per 100 ml of diluent. A 5% solution contains 5 g anesthetic per 100 ml diluent, or 50 mg per ml. Dosages of injectable anesthetics, as with all drugs, should be calculated in milligrams and not in cubic centimeters since concentrations of various preparations may be different.

Intramuscular Route (69, 87G)

Intramuscular injections are made into the heavily muscled areas of the body, the most common site being the rectus femoris muscle of the hind leg. The sciatic nerve should be avoided. Before injecting, care must be taken that the needle is not in a vessel since some medications are extremely toxic if injected by the intravascular route, especially arterial. If blood enters the syringe when the plunger is withdrawn, the needle should be withdrawn and placed in a new site.

Anesthetics such as the dissociative agents and certain tranquilizers and narcotics may be safely administered by the IM route. In the past, barbiturates have been administered IM because of insufficient knowledge of the IV technic; but the IM route is not recommended for these agents. The barbiturates are very irritating to tissues and are impossible to titrate by any route other than IV. The onset of barbiturate anesthesia when administered IM is from 15 to 30 minutes following injection.

Intraperitoneal Route (69, 87G)

The injection site, lateral to the umbilicus, is shaved and disinfected. A local anesthetic should be infiltrated into the injection site. An assistant holds the animal in a vertical position so that the abdominal organs descend toward the pelvic cavity. This route is not recommended because anesthetics cannot be titrated, absorption is slow and variable, and there is danger of injecting the anesthetic into one of the abdominal organs.

Intrapleural Route (69, 87G)

The injection site is low in the 8th or 9th intercostal space. This route is not recommended. Besides the disadvantages of the intramuscular and intraperitoneal route for barbiturates, considerable pathology to the pleura, lungs, and heart may be produced.

Subcutaneous Route (SubQ)

The subcutaneous region is located between the skin and muscles. A fold of skin is held between the thumb and index finger and elevated. The needle is inserted up to the hub into the fold of skin. The skin fold may be released once the needle has been inserted.

INHALATION ANESTHESIA EQUIPMENT

There are a number of technics and types of equipment for administering inhalation anesthesia; the choice for laboratory animals depends on the animal (body size, circulation, respiration) and the anesthetic agent. The following anesthetic systems will be discussed:

1. Semiopen
    a. Open drop
    b. Boxes and chambers
    c. Ayre's T tube
    d. Magill
    e. Masks
    f. Insufflation
2. Nonrebreathing

    Digby Leigh and Stephen Slatter valves
3. Rebreathing
    a. To-and-fro
    b. Circle (closed and semiclosed)

Semiopen Systems

The respiratory system is open to the atmosphere on both inspiration and expiration. The degree of rebreathing exhaled gases depends upon fresh gas flow into the system. Open-drop and chamber systems are seen in Figure 3.

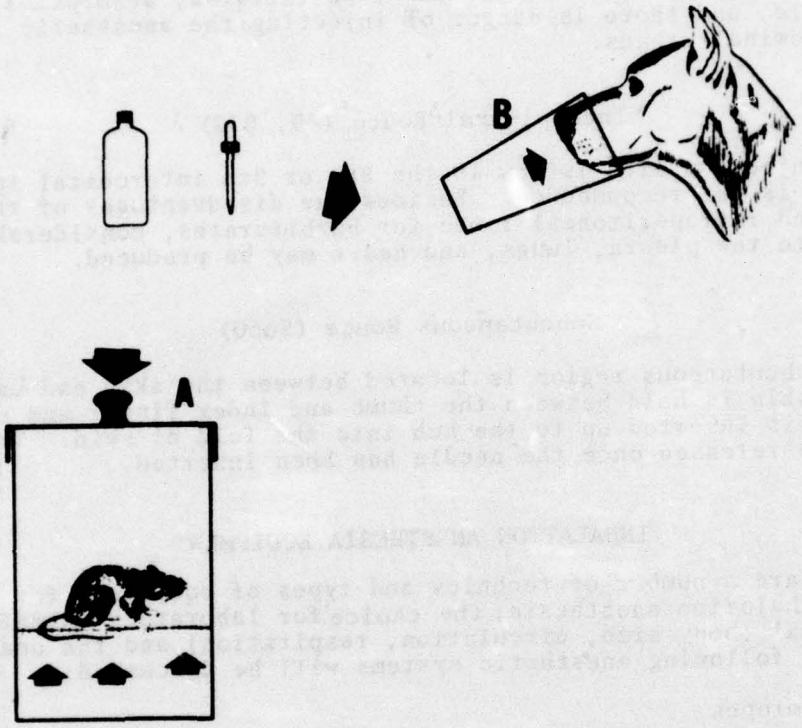

Figure 3. Semiopen systems: A--Anesthetic chamber; B--Open-drop technic.

Open Drop (69, 122)

Equipment: Wire mesh mask is covered with 8 layers of 16-ply surgical gauze or a cone is loosely filled with cotton to permit unrestricted air flow during respiration.

Technic: Liquid anesthetic is dropped slowly and evenly over the entire mask or cone. Initially the mask is held slightly away from the face. As induction proceeds, the mask or cone is placed directly over the nose and face to minimize dead space. If breath-holding occurs, the mask is removed completely from the face to prevent the accumulation of a high concentration of anesthetic from being inhaled when the animal resumes respiration. Diethyl ether is the agent most commonly used. Methoxyflurane may be used for small animals such as rodents. Halothane is not recommended because of its potency and the wastefulness of this technic.

Advantages:

1. No valves, therefore little respiratory resistance.

2. Suitable for small, easily restrained animals.

Disadvantages:

1. Uneconomical, wastes anesthesia.

2. Variation in anesthetic concentration.

3. No method to support ventilation.

4. Exhaled CO_2 that accumulates in dead space may be rebreathed unless a source of oxygen is introduced under the mask.

5. Danger of combustion when flammable anesthetics such as ether are used.

Boxes or Chambers--

Equipment: A pledget of cotton soaked with anesthetic may be placed in a Bell jar or beaker that has a lid. The Bell jar should have a wire floor between the animal and cotton to prevent direct contact with the liquid anesthetic.

Airtight chambers possess inherent dangers in that the anesthetic concentration varies depending on the size of the box, temperature, and tidal volume. The animal can become anoxic unless oxygen is supplied. Ideal anesthetic chambers for small laboratory animals have been adapted to utilize precision vaporizers and allow adequate circulation between the chamber and carbon dioxide absorber (11, 16, 119).

Technic: Diethyl ether or methoxyflurane may be safely administered in a Bell jar. The animal is left in the jar until the desired level of anesthesia is achieved. Potent anesthetics such as halothane require precision vaporizers.

Advantages: Ideal for anesthetic induction of rodents and small animals that are difficult to restrain.

Disadvantages: Vary with the complexity of the system. The simple Bell jar presents problems of hypoxia, hypercarbia, and unknown anesthetic concentration.

Ayres T Tube (60, 69, 121, 122)--

Equipment: Consists of a T-shaped tube with inspiratory and expiratory arms (Fig. 4). The inspiratory arm is connected directly to the endotracheal tube. The gas source is delivered from a vaporizer. The basic T-tube may be modified as follows:

1. Reservoir tube. Gases are inspired from both the inspiratory and expiratory arms. To prevent rebreathing of expired gases and provide proper elimination of carbon dioxide, a reservoir tube can be

attached to the expiratory arm. The reservoir tube should be one-third the animal's tidal volume.

2. Rebreathing bag. The reservoir bag attached to the expiratory arm aids in positive pressure ventilation and increases the capacity of the reservoir tube.

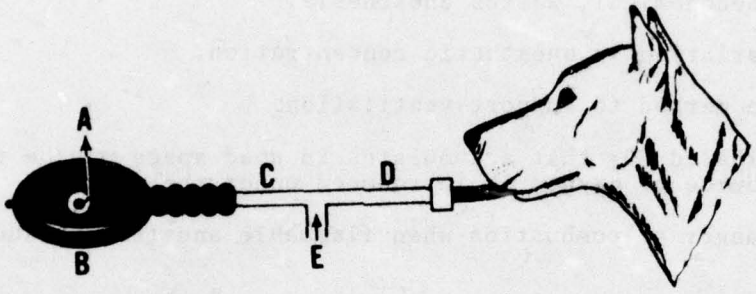

Figure 4. Ayres T-tube: A--Outflow vent; B--Reservoir bag; C--Expiratory arm; D--Inspiratory arm; E--Gas source.

Technic: The Ayres T tube is recommended for animals below 5 kg in weight. Rebreathing of exhaled gases will not occur if the oxygen flow is greater than the respiratory minute volume. When a reservoir tube is used, the gas flow should be 2.5 times the respiratory minute volume, and 3 times the minute volume when a reservoir bag is attached to minimize rebreathing. A cuffed endotracheal tube enables positive pressure respiration when the open end of the reservoir limb or the exhaust port on the reservoir bag is occluded.

Advantages:

1. No valves are present; therefore, low respiratory resistance.

2. Dead space is minimal in the small T-tube.

3. Anesthetist can rapidly control the anesthetic concentration.

Disadvantages: Expensive because of high gas and anesthetic flow rates.

Magill System (18, 60, 69, 122)--

Equipment (Fig. 5): Consists of a reservoir bag with a capacity of 8 times the tidal volume, exhalation pop-off valve located as close to the animal as possible, flexible hose, and vaporizer.

Technic: When the animal exhales and the reservoir bag is maximally distended, the alveolar gas containing high CO_2 is at the level of the pop-off valve and is vented into the atmosphere. Adequate gas flow is needed to prevent rebreathing and to flush gases rich in CO_2 into the atmosphere. The recommended gas flows are 2 liters/min for animals up to 40 lb (18 kg) and 4 liters/min for animals weighing more than 40 pounds.

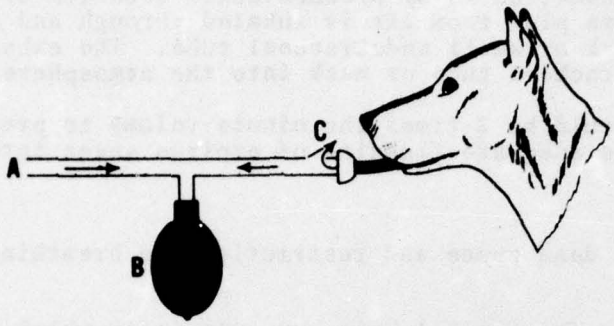

Figure 5. Magill system: A--Gas source; B--Reservoir bag; C--Exhaust valve.

Advantages:

1. Only one exhaust valve with little resistance to respiration.

2. Minimal rebreathing when gas flow exceeds respiratory minute volume.

Disadvantages: Expensive because of high gas and anesthetic flow rates.

Masks (69, 81, 122)--

Equipment: A number of masks made of rubber, metal, or plastic are available commercially. Transparent plastic masks are an advantage in that the anesthetist can observe the animal's face. Masks designed for cats can be used for rabbits and guinea pigs. The end of a Y-piece can be placed over a bird's beak and used as a mask. Masks should provide a good seal and contain minimal air space (dead space).

Technics: The animal is restrained as gently as possible, and the mask is placed near the face. The initial anesthetic concentration is low. As the animal becomes increasingly sedated, the anesthetic concentration is increased and the mask is placed snugly over the nose and mouth. Induction is begun with 75% nitrous oxide and 25% oxygen, followed with halothane or methoxyflurane. Halothane is started at 0.25% and gradually increased by 0.5% increments up to 2%-4%. Following induction the nitrous oxide is reduced to 50% and halothane is adjusted to a maintenance dose of 1%-2.5%. A similar technic is used with methoxyflurane, with induction concentration increasing by increments up to 1.5% and maintenance at 0.25%-0.75%.

Insufflation (69)

Equipment: Vaporizer, delivery tube, mask, or small endotracheal tube without a cuff. The airway must not be restricted.

Technic: Induction is by preanesthetic sedation or mask. The anesthetic mixture plus room air is inhaled through and around the loose-fitting mask or small endotracheal tube. The exhaled gases pass around the endotracheal tube or mask into the atmosphere.

Gas flow should be 2 times the minute volume to prevent rebreathing and to enable adequate flushing of expired gases into the atmosphere.

Advantages:

1. Minimal dead space and restrictions to breathing if the catheter is small.

2. Suitable for small laboratory animals in which dead space and airway resistance are critical factors.

Disadvantages:

1. Waste of gas and anesthesia.

2. Loss of body heat and airway moisture.

3. Inability to control or assist breathing.

4. Unknown anesthetic concentration due to dilution with room air.

Nonrebreathing Systems (60, 69, 121, 122)

These systems contain both an inhalation and exhalation valve, which prevents mixing the anesthetic mixture with atmosphere or exhaled gases.

Equipment--There are several basic designs (Ruben, Lewis-Leigh, Digby-Leigh, Stephen-Slater). Equipment includes vaporizer, reservoir bag, inhalation and nonrebreathing exhalation valves, and endotracheal tube. The reservoir bag is located between the vaporizer and the nonrebreathing valve.

Technic--This technic is ideal for animals weighing less then 7 kg. The gas flow is adjusted so that the reservoir bag does not completely collapse on inspiration. If the gas flow slightly exceeds the minute respiratory volume, rebreathing is minimal. Excess gases will leak out through the low-resistance expiratory valve. Respiratory assistance is achieved by closing the exhalation valve and manually compressing the reservoir bag.

Advantages:

1. No accumulation of carbon dioxide.

2. Rapid induction; inhaled anesthetic mixtures are not diluted by exhaled gases.

3. Small dead space, only up to inhalation valve.

4. Lightweight valves produce minimal respiratory resistance.

Rebreathing Systems (60, 69, 121, 122)

The rebreathing systems are classified as closed or semiclosed. In the closed system there are no leaks, and only fresh gases in amounts necessary to supply the animal's metabolic needs and maintain anesthesia are added. In the semiclosed system, part of the exhaled gases are passed back into the system and part escape into the atmosphere. With high oxygen flows, the semiclosed system approaches a nonrebreathing system, with most of the expired gases being flushed through the pop-off valve out of the system. For both the closed and semiclosed systems, the carbon dioxide is chemically removed from the exhaled gases before they are rebreathed.

Two basic types of anesthetic machines are used, the to-and-fro and the circle systems.

To and Fro (69, 122)

Equipment: A reservoir bag, CO_2 absorbent canister, pop-off valve, inlet for fresh gases, flow meter, and vaporizer (Fig. 6).

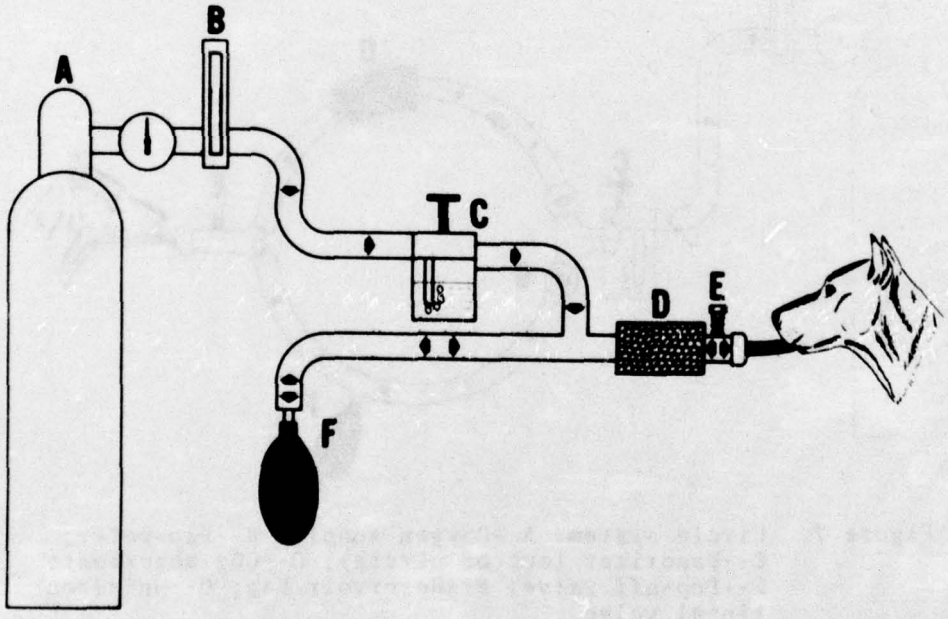

Figure 6. To-and-fro rebreathing system: A--Oxygen supply; B--Flowmeter; C--Vaporizer; D--CO_2 absorbent; E--Pop-off valve; F--Reservoir bag.

Advantages:

1. Efficient CO_2 absorption since both inspired and expired gases pass through the soda lime.

2. Conservation of body heat and moisture.

3. Rebreathing bag convenient for anesthetists.

4. Valves are not necessary.

Disadvantages:

1. Dead space with animals weighing less than 30 lb (14 kg).

2. Heat produced by the CO_2 absorber (its proximity may allow the animal to become overheated).

Circle (60, 69, 121, 122)--

Equipment: A reservoir bag, CO_2 absorbent canister, unidirectional inhalation and exhalation valves, breathing tubes with a Y-piece, inlet for fresh gases, pop-off valve, and pressure manometer (Fig. 7).

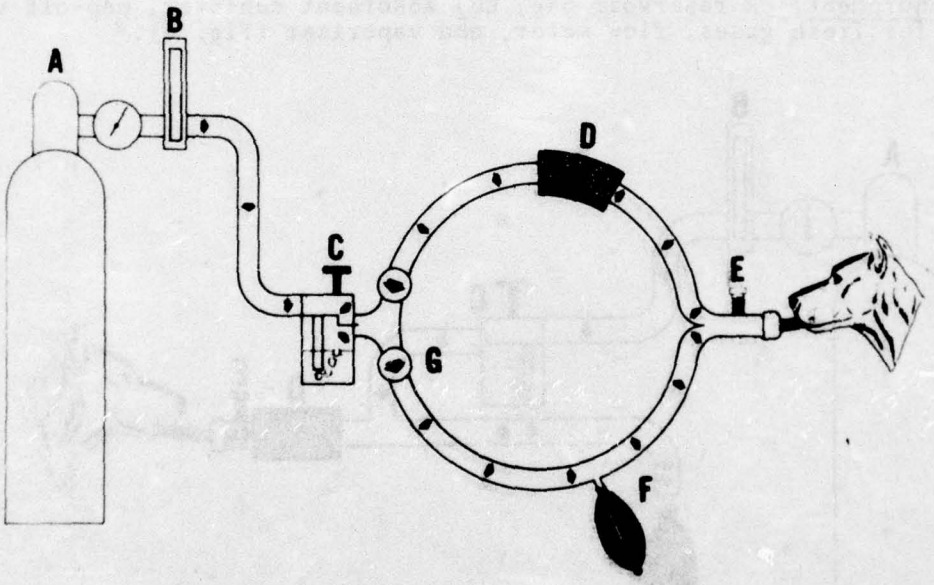

Figure 7. Circle system: A--Oxygen supply; B--Flowmeter; C--Vaporizer (out of circle); D--CO_2 absorbent; E--Pop-off valve; F--Reservoir bag; G--Unidirectional valve.

Advantages:

1. Conservation of body heat and moisture.

2. Economical use of anesthesia.

Disadvantage: Dead space is large for small animals.

CO_2 Absorbent Canister (121)

In a rebreathing system, the carbon dioxide generated by the patient must be removed; for this, a CO_2 absorbent canister containing either soda lime or Baralyme is used. Soda lime is a mixture of sodium and calcium hydroxide. Baralyme consists of barium and calcium hydroxide; it produces less heat and is less caustic than soda lime. In the canister, CO_2 combines with water to form carbonic acid which is neutralized by OH^-.

The average canister is effective for 3-6 hours of continuous anesthesia, depending on the size of the animal. Most CO_2 absorbers contain an indicator that changes color as the chemicals are exhausted (usually from white to pink to violet); however, this color change may revert on standing to a "safe" color, so the color of the chemicals can be misleading. The chemicals should be examined after each use and replaced if one-half has changed color. Active absorbents can be easily crumbled between the fingers; with loss of activity, they become hard and brittle carbonate salts.

If the absorbent becomes exhausted during a surgical procedure, the patient will become hypercapnic (elevated CO_2) without signs of cyanosis since adequate O_2 is being administered (69). Elevated CO_2 levels, if uncorrected, will produce acidosis, cardiac arrhythmias, and eventually cardiac arrest. Signs observed during hypercapnia are elevated heart rate and blood pressure which may produce increased bleeding at the surgery site. The respiratory tidal volume may also increase. These signs may be misinterpreted as indicating the patient is not receiving adequate anesthetic. A further increase in anesthetic at this time, combined with the elevated CO_2, would cause the adverse effects to progress at a faster rate.

The following recommendations have been made for proper packing of the canister to increase the efficiency of the absorbent (122):

1. The canister should be tapped gently as it is being filled to permit maximum filling. Open spaces do not absorb CO_2 and let it be recirculated to the patient.

2. The opening through which the absorbent is poured should be large enough to prevent fragmentation of the granules.

3. Supply stocks of the absorbent should be resealed tightly. The moisture content of the absorbent is important because CO_2 must combine with water to form carbonic acid.

4. The canister should not be filled with an absorbent that is too dusty. After the canister is filled, dust should be removed by blowing through the canister.

Vaporizers (121)

The concentration of a volatile anesthetic agent delivered from a vaporizer depends on several factors: (1) the characteristic vapor pressure of the anesthetic agent and the liquid temperature; (2) the evaporation surface of the vaporizer; (3) the level of the anesthetic agent; and (4) the flow of the carrier gas through the vaporizer.

The saturated vapor pressure varies with the liquid temperature, increasing as temperature rises. As the saturated vapor is removed from the vaporization chamber and evaporation takes place, the liquid temperature falls. This will change the pressure of the saturated vapor and less will be available for dilution; therefore, one of the most important functions of a vaporizer is to maintain a constant liquid temperature, despite the cooling process of vaporization.

The evaporation surface of a vaporizer can vary with design. In the more simple glass vaporizers, it may be limited only to the gas-liquid interface created by the diameter of the bottle. Under this small interface, the output of the vaporizer will be limited. The vaporization surface can be increased without enlarging the vaporizer by placing a series of wicks into the vaporization chamber, thus increasing the surface area for evaporation, or by placing a bubbler in the system, enabling the gas to bubble through the liquid anesthetic.

A disadvantage of the glass vaporizer is that the concentration of anesthetic vapor delivered is not constant and will vary with the flow of oxygen, the temperature of the anesthetic liquid, and the amount of liquid anesthetic contained within the vaporizer. When a high gas flow is used, the temperature of the anesthetic liquid will decrease rapidly during vaporization unless an external source of heat is provided; a drop in concentration of vapor parallels the temperature change. The thermal conductivity of glass is poor, and heat is not readily conducted into the liquid. A more constant temperature can be maintained by adding an external source of heat or by substituting a metal container for the glass container (Copper Kettle). If temperature changes can be prevented, a constant output can be anticipated from any vaporizer.

The deficiencies of the glass vaporizers are partially eliminated in the precision vaporizers (the thermocompensated vaporizers and the "heat sink" vaporizers; i.e., Fluotec, Pentec, Fluomatic, Pentomatic, and Ethermatic vaporizers). These enable delivery of a controlled concentration of anesthetic vapor for a long time, independent of ambient temperature and carrier gas flow.

Vaporizers for halothane must be finely calibrated since halothane has high vapor pressure and is highly volatile. High concentrations can be obtained even at low oxygen flows. The following vaporizers are used for delivering halothane (122):

1. Fluotec Mark I (Fraser Sweatman, Inc.): temperature compensated. Dial settings for percent delivery do not correlate well with output concentrations when flow rates are below 4 liters/min.

2. Fluotec Mark II (Fraser Sweatman, Inc.): both temperature and flow compensated. Consistent concentrations of halothane are delivered at both high and low gas flows.

3. Fluomatic (Foregger): temperature and flow compensated. Good correlation between anesthetic concentration and dial settings at flow rates above 1 liter/min.

4. Copper Kettle (Foregger): anesthetic concentration determined by a slide-rule calculator containing variables for total gas flow, gas flow delivered to the vaporizer, anesthetic partial pressure, and vaporizer temperature.

Methoxyflurane has a low vapor pressure and needs a large surface area or a high gas flow to deliver adequate concentrations of anesthetic. Methoxyflurane may be safely delivered by nonprecision vaporizers or the open-drop technic. The following vaporizers are used for delivering methoxyflurane:

1. Pentec (Fraser Sweatman, Inc.): calibration curves established for gas flows of 5 liters/min. Gas flows for small animals are usually below 5 liters.

2. Pentomatic (Foregger): similar to the Fluomatic.

3. Copper Kettle (Foregger): excellent for methoxyflurane.

4. Glass vaporizers designed for diethyl ether are satisfactory for methoxyflurane. They are uncalibrated; therefore, the anesthetic concentration is unknown.

The vaporizer may be located either within or out of the circle. In-circle vaporizers utilize the animal's tidal volume to vaporize the anesthetic, while out-of-circle vaporizers use fresh oxygen being delivered to the circle. The out-of-circle vaporizers possess a number of advantages over the in-circle.

Table 1 compares the effects of ventilation, fresh gas flow, and different types of vaporizers with the location of the vaporizer (out-of-circle or in-circle) (122).

Troubleshooting

If the patient fails to go under anesthesia, the following areas should be checked:

1. Endotracheal tube in esophagus. Palpate esophagus or visually examine the pharynx. The patient will usually cough when tube is in larynx during induction period. If an animal that has been intubated is making any kind of sound, such as whining or snoring, the endotracheal tube may be misplaced and should be checked and repositioned properly. In a properly intubated animal, the larynx and oral cavity are bypassed and no sound can be made.

2. Anesthetic level in vaporizer too low. The anesthetic should be above bottom of wick in a methoxyflurane vaporizer. When filling vaporizer, disconnect from patient to prevent an excessively high anesthetic concentration being given.

3. Defective valve in vaporizer allowing oxygen to bypass. The anesthetic odor should be noticeably stronger when the vaporizer is turned on high.

4. Inhalation breathing tube disconnected from vaporizer or endotracheal tube.

5. Oxygen turned off.

6. Water on vaporizer wick (methoxyflurane), usually caused by maintaining too low a level of anesthetic in vaporizer.

7. Hypercarbia (excessive CO_2 in blood). CO_2 absorber is defective or not full, or ventilation is poor.

If the patient is under anesthesia too lightly even with vaporizer turned on full, check the following:

1. Endotracheal tube down too far. The tube may be into one bronchus and delivering anesthetic to only one lung.

2. Endotracheal tube too long. If the tube extends very far beyond incisors, it will produce excessive dead air space. This may be critical in small animals.

3. Too small an endotracheal tube. The largest size that will conveniently pass into the trachea should be used.

4. Cuff on endotracheal tube not inflated or not inflated adequately. If the cuff is not inflated properly, you can hear air exhaled from larynx around the tube and detect odor of the anesthetic agent from the patient's mouth.

5. Bypass valve in vaporizer not working properly, allowing too much oxygen to bypass the vaporizer.

6. Broken gasket or leaking gasket on vaporizer jar (methoxyflurane).

7. Leak around soda-lime canister.

8. Leaks around breathing tubes, rebreathing bag, or holes in the bag.

9. Leak around the connector.

10. Y connector valve may be open.

11. Valves sticking (interrupts circle breathing).

12. Water on vaporizer wick (methoxyflurane).

TABLE 1. COMPARISON OF IN-CIRCLE AND OUT-OF-CIRCLE LOCATIONS

Vaporizer out of circle	Vaporizer in circle
Ventilation	
a. Changes in ventilation will not affect the output of the vaporizer.	a. Sudden changes in ventilation can produce dangerously high inspired concentrations.
b. An increase in ventilation will reduce inspired concentration because of an increased uptake of anesthetic agent by the animal and a constant output of the vaporizer.	b. An increase in ventilation due to light anesthesia will automatically increase the inspired concentration.
c. Assisted or controlled ventilation can be used with a greater degree of safety.	c. Assisted or controlled ventilation at any given setting will greatly increase inspired concentrations.
Fresh Gas Flow	
a. For any setting, the lower the fresh gas flow, the lower will be the inspired concentration being delivered from the vaporizer. The lower the fresh gas flow, the greater the economy.	a. For any setting, the lower the fresh gas flow, the higher the inspired concentration. The lower the fresh gas flow, the greater the economy.
b. Economy does not introduce the risk of high concentrations.	b. Economy is at the expense of potentially high inspired concentrations.
Vaporizer	
a. High-efficiency vaporizers are essential.	a. Low-efficiency vaporizers can be used.
b. Known concentrations can be delivered to the breathing circuit, and an estimate of the inspired concentrations can be made with no difficulty.	b. Calibrated vaporizers are meaningless because ventilation affects the inspired concentration to a marked degree.

Equipment Maintenance

Prior to Use--A routine functional check should be performed before each procedure.

1. Check the O_2 and N_2O sources to assure adequate gases to complete the contemplated procedure. Turn on the valves and check the flowmeters for proper operation.

2. Assure that there is adequate volatile anesthetic agent in the vaporizer. The fluid level should cover the wick or bubbler (methoxyflurane).

3. Check the CO_2 absorber (soda lime or Baralyme) for level and color change to assure adequate CO_2 absorption.

4. Check the one-way valves by inhaling and exhaling through the trachea tube adapter. These valves can stick.

5. Check the pop-off valve. It should be open unless thoracic surgery is contemplated.

6. Check the endotracheal tube for cleanliness, correct size, patency, and a functional inflatable cuff.

After Use--A routine procedure should be performed.

1. Turn vaporizer control to OFF.

2. Turn gas (O_2 and N_2O) pressure valves to OFF. They should be closed tightly or the gases will escape through the flowmeter valve. Note: Always turn off the pressure valve before turning off the flowmeter valves.

3. Turn off the flowmeter control valves. These controls are fine needle valves made of soft brass and should be only finger tight. Excessive tightening deforms the valve, causing incorrect flow, and will not prevent the gases from escaping while the machine is not in use if the pressure valve is inadvertently left on.

4. Check the CO_2 absorber and replace it if the color change is extensive. The color change is best checked at the end of a procedure because some of the color will change back before the machine is used again.

5. Refill vaporizer (methoxyflurane or halothane) with correct amount of agent. (If ether, discard at end of 1 day's use.) The volatile agents cause deterioration of rubber and plastic parts of the anesthetic machine; these agents should be drained from the vaporizer and the removable tubing flushed when the machine is not in use.

6. Cover the machine to avoid dust accumulation which may alter efficient operation (especially if the machine is not used frequently).

7. Keep machine, controls, and all accessories clean and free of blood and hair. The preservative in halothane and methoxyflurane

leaves a sticky residue that will cause valves to stick. The vaporizers should be flushed weekly with ether to dissolve the residue.

8. Flush or brush endotracheal tube after each procedure. Avoid getting water into the cuff. Do not immerse the tube in water; the cuff will stick and may not inflate properly. There have been reports of infectious tracheitis spread by dirty endotracheal tubes.

INHALATION ANESTHESIA TECHNIC

Halothane

Premedicate--Atropine (0.04 mg/kg) or scopolamine (0.01-0.02 mg/kg), alone; or atropine or scopolamine, plus dissociative agents (primates), narcotics, or tranquilizers as desired.

Denitrogenate--100% O_2 for 2-3 minutes with frequent bag flushes.

Induct--

1. With a mask:

a. Up to 80% N_2O (increased slowly to 80%) and 20% O_2 for no longer than 2-3 minutes (to prevent induction hypoxia), followed by:

b. 50% N_2O and 50% O_2 with 3% halothane, given until intubation is possible (swallowing reflex abolished).

c. Intubate and continue induction until the desired surgical stage of anesthesia is reached.

2. With a barbiturate: After induction with an IV barbiturate, intubate, denitrogenate, and go straight to maintenance levels of gas anesthetic.

Maintenance--35%-50% N_2O and 50%-65% O_2 with 0.5%-2% halothane (i.e., 35% N_2O and 65% O_2 plus the desired concentration of halothane; up to 50% N_2O and 50% O_2 with the desired concentration of halothane to maintain surgical anesthesia). Total gas flow should be high enough so that the bag occasionally requires emptying. Oxygen flow should be high enough to supply the patient's metabolic requirements.

Recovery--About 10 minutes from complete closure of the skin incision, turn off the halothane and maintain patient on 35%-50% N_2O and 50%-65% O_2. When the skin incision is closed, turn off the N_2O and maintain on 100% O_2 for at least 2-3 minutes (to prevent diffusion hypoxia from the N_2O leaving the body rapidly); then after the first 2-3 minutes of bagging with 100% O_2 to keep the patient well ventilated, stop bagging and allow CO_2 to build up in the patient until spontaneous respiration returns. (May require 2-3 minutes with only an occasional squeeze on the bag before CO_2 will build up enough to start the respiratory drive.) A Pa_{CO_2} slightly higher than normal may be required due to an increased threshold of the drive mechanism to CO_2. An occasional animal may not return to spontaneous respiration within a few minutes, and a respiratory stimulant may be helpful in such instances.

After spontaneous respiration returns, turn off the gases and complete the routine for shutting down the anesthesia machine. Extubate the patient when the swallowing reflex returns.

Methoxyflurane

The technic for administering methoxyflurane is similar to that for halothane. Methoxyflurane may be used in a glass bubble-through or wick vaporizer. Since 3%-4% is the highest concentration possible at room temperature, the vaporizer is turned on high until surgical anesthesia is attained. Then the concentration is turned down for maintenance. Glass vaporizers are not calibrated. The numbers on them (1-10) only show the direction to turn the valve to increase or decrease the anesthetic concentration. Since the solubility of methoxyflurane is greater than that of halothane, induction, recovery, and changes in anesthetic level will be slower than with halothane.

VENTILATING THE ANESTHETIZED PATIENT

Normal respiration is passive. The intrapleural pressure is always subatmospheric and fluctuates with the respiratory cycle (Fig. 8). The negative pleural pressure relative to atmospheric pressure varies from -4 to -8 cm H_2O at the height of inspiration and from -2 to -4 cm H_2O at the end of expiration as the chest wall expands and contracts. The elastic lungs expand as the intrapleural pressure decreases, allowing air to passively enter the lungs. Expiration is due to passive relaxation of the chest.

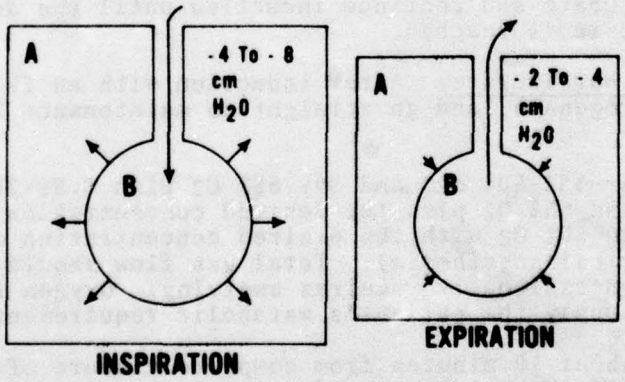

Figure 8. Passive ventilation. Pleural pressures are subatmospheric compared to lung pressures.

When general anesthesia is induced, respiration becomes shallow and weak and alveolar units begin to collapse. The reflex-induced large breath (yawn or sigh) disappears or is infrequent and ineffective. During surgery the position of the patient and the use of retractors may further interfere with respiration. It is important that the anesthetist maintain the structural integrity of the lung by replacing the

yawn with intermittent deep inflations and by augmenting the tidal volume. Tidal volumes of 6 ml/kg are probably adequate to prevent the collapse of the lung and the development of atelectasis.

Physiological dead space consists of the tracheobronchial tree (anatomical dead space) and nonperfused alveoli (alveolar dead space) where gas exchange does not take place. The gases composing the physiological dead space, which are inhaled and exhaled with each breath, do not contribute to respiratory exchange and constitute wasted ventilation. The anesthetist may increase this dead space during anesthesia. Premedication with atropine may increase the anatomical dead space by 20% to 50%, depending on the state of the vagal tone and the dose administered. Masks used for induction of anesthesia and other respiratory apparatus constitute variable additions to mechanical dead space, while the process of tracheal intubation eliminates a large fraction of the anatomical dead space (unless the tube is too long). Generally, the reduction in dead space by tracheal intubation is of the same order as the increase in dead space due to the effects of anesthesia. The respiratory dead space constitutes 30%-40% of the tidal volume for normal or increased tidal volumes. In spontaneously breathing animals, however, the effect of general anesthesia is usually to decrease the tidal volume, and in these circumstances the effective dead space or wasted ventilation may constitute more than half of the tidal volume. A large dead space combined with shallow respiration (small tidal volume) results in the animal rebreathing the same gases which it has attempted to exhale. It is generally better to ventilate at a tidal volume larger than indicated and at a slower respiratory rate than the awake animal selects.

The anesthetist can provide adequate arterial oxygenation without ventilating the patient by enabling 100% oxygen to flow into the lungs. Ventilation, however, is still required to remove carbon dioxide. The tension of carbon dioxide in the blood (PCO_2) can be used to measure the efficiency of ventilation. When the animal is hyperventilated, carbon dioxide is removed from the body faster than it is being produced, resulting in respiratory alkalosis (low P_{CO_2}, high pH). Carbon dioxide removed at a rate less than the rate of metabolic production, because of hypoventilation, results in respiratory acidosis (high PCO_2, low pH). Changes in pH may lag behind those of the P_{aCO_2} because of renal compensation (i.e., change in rate of excretion and retention of HCO_3^- and/or H^+). Small immediate changes in acid-base balance are controlled by the lungs, while larger long-term changes are controlled by the kidneys. Ventilation during anesthesia is, thus, a breath-by-breath control of the patient's acid-base balance.

Considerable resistance to breathing is added by any breathing circuit used during anesthesia. The best modern circle rebreathing systems--with jumbo-size carbon dioxide canisters and large-bore corrugated tubing and low-resistance, lightweight, one-way valves--double or triple the overall resistance to breathing. Nonrebreathing circuits with the valves designed for man are only slightly better.

To minimize alveolar collapse, hypoxia, and acidosis, the tidal volume should be large. The lightly anesthetized animal commonly breathes rapidly and shallowly. These factors constitute a strong

argument for assisted or controlled respiration during balanced general anesthesia. The rate of ventilation should be monitored by determining arterial pH and blood gases to prevent an acid-base imbalance from developing.

"Intermittent Positive Pressure Breathing" (IPPB) is the term used to describe positive pressure respiration produced by manually squeezing a reservoir bag or by using a respirator. With IPPB, the animal's respiration can be assisted or controlled. With assisted respiration the animal breathes spontaneously; the anesthetist occasionally increases the tidal volume by squeezing the reservoir bag every 20-30 seconds. Assisted respiration dilates the alveoli, which may have collapsed, and assists in removing carbon dioxide. The anesthetist initiates controlled respiration by ventilating the animal to lower the P_{CO_2} to a level where it no longer stimulates the respiratory drive mechanisms. The animal ceases to breathe on his own and the anesthetist "breathes" for him.

Positive pressure respiration may alter venous circulation to the heart. The intrapleural pressure is relatively negative during unassisted inspiration (-6 cm H_2O) compared to expiration (-2 cm H_2O). Venous return and cardiac output increase with inspiration because of decreased external pressure on the thin-walled veins in the thoracic cavity and lungs. When respiration is assisted by positive pressure, the lungs dilate by internal pressure. At 20 cm H_2O pressure, the lung capillaries are closed and venous return to the heart is greatly reduced, adversely affecting cardiac output.

When a thoracic incision is made, the subatmospheric pressure in the chest equalizes with the atmosphere; therefore, the pressure on the inside of the lungs is the same as that on the outside (Fig. 9). Under these conditions, the expansion and contraction of the chest wall has no effect on the intrapleural pressure; for adequate ventilation, air must be forced into the lungs by means of positive pressure ventilation.

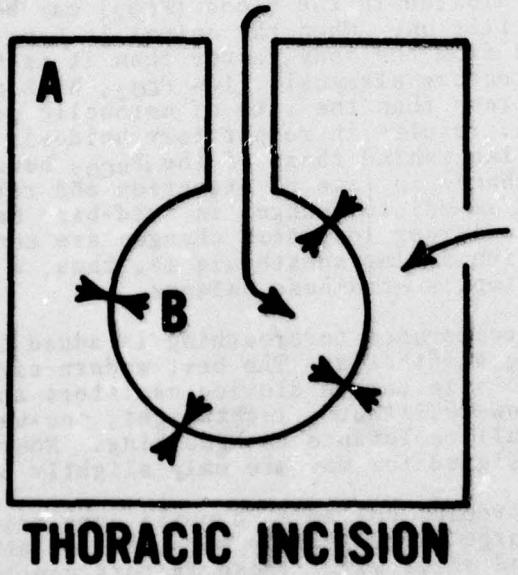

Figure 9. Thoracic incision. Pleural (A) and lung (B) pressures are equal. Positive pressure ventilation is required for ventilation.

The following guidelines should be used when respiration is controlled in an anesthetized animal:

1. Divide the respiratory cycle into a ratio of inspiration (1/3) and expiration (2/3) to ensure an adequate time interval for venous return during expiration.

2. Produce inspiration by a rapid strong squeeze on the reservoir bag to bring the inspiratory pressure up to 15 cm H_2O. Then release the bag immediately so that the pressure returns to zero, thereby increasing the time period for venous return. An animal should not be bagged at pressures over 20 cm H_2O unless for a specific reason, such as reinflating an atelectatic lung after it has been packed off.

3. For a dog, the respiratory (bagging) rate should be between 15-20/min. The rate should not be more than 20/min unless intentional hyperventilation is desired, as for brain surgery where a deliberate respiratory alkalosis (low P_{CO_2}) may be desired to decrease blood flow to the brain and surgical field. The optimum respiratory rate will vary with the species and surgical procedure.

Respiratory volumes for laboratory animals have been measured and a formula was derived which gives a relatively satisfactory correlation between weight and respiratory volume: Respiratory volume per minute in cubic centimeters = 2.10 x weight (grams).

The average respiratory volumes that were measured were: (47)

	Wt (g)	Resp/min	Tidal air (cm^3)	Resp vol/min (cm^3)	
				Actual	Calculated
Mice	19.8	163.4	0.15	24.5	19.9
Cotton rats	76.8	94.5	0.35	39.6	55.5
Hamsters	91.6	73.6	0.83	60.9	62.1
White rats	112.8	85.5	0.87	72.9	72.9
Guinea pigs	466.0	90.3	1.75	155.6	210.6
Rabbits	2069.0			800.0	634.0
Monkeys	2682.0	40.0	21.2	863.0	785.0

Tidal volume has been calculated by multiplying the factor 0.0062 x body weight (1).

MONITORING ANESTHESIA

For safe administration of general anesthetics, the patient must be observed for various changes in reflexes. A somewhat predictable sequence of events occurs from the early stages of anesthesia to the stage of complete medullary paralysis with respiratory or cardiac arrest. Unfortunately, the sequence of signs indicating depth of anesthesia will vary between the individual patient, species, type of anesthetic, and preanesthetic agents.

Determination of anesthetic depth is important in establishing criteria for safe anesthesia. Many reflexes and the relaxation of certain muscle groups occur at various levels of anesthesia, and being aware of the cessation of function of these protective reflexes is important in anesthetic management.

The sequential effects of increased arterial concentrations of a general anesthetic are:

1. Analgesia and amnesia.
2. Loss of consciousness and motor coordination.
3. Reduction of protective reflexes.
4. Blockage of afferent stimuli.
5. Muscular relaxation.
6. Respiratory and cardiovascular depression.
7. Depression of cardiovascular and respiratory reflexes.
8. Apnea.
9. Cardiac standstill.

The depth of anesthesia may also be classified by four stages:

1. Induction and analgesia.

    a. Beginning of anesthesia to the loss of consciousness

    b. Analgesia and consciousness with disorientation (subjective in nature and can be related only to man)

2. Delirium or involuntary movement.

    a. Loss of consciousness and subsequent excitement (delirium and uninhibited actions).

3. Surgical anesthesia. Divided into planes or levels characterized by a progressive depression of respiration, circulation, protective reflexes, and muscle tone.

4. Death. Respiratory arrest followed by circulatory arrest.

The following systems and reflexes are monitored to control the depth of anesthesia.

Cardiovascular System

Cardiac Auscultation--With esophageal stethoscope or stethoscope positioned on the chest wall, listen to type, characteristics, and change of heart sounds.

Heart or Pulse Rate--Determine every 10-15 minutes. Cardiac monitors which respond to high-voltage R waves (beepers) are frequently used. Such monitors indicate only the heart rate; they do not give early warning of many impending conditions, nor do they differentiate between fibrillation and cardiac standstill.

Arterial Blood Pressure--Measurement can be direct (intra-arterial catheter to mercury manometer or pressure transducer) or indirect (sphygmomanometer). Pressure is the product of cardiac output and peripheral arterial resistance ($P = CO \times R$). Peripheral resistance frequently maintains a deceptively normal arterial pressure during low-cardiac-output shock.

Central Venous Pressure--CVP can be measured with a water manometer connected to a centrally positioned intravenous catheter and indicates the effectiveness of the cardiac pump in relation to the circulating blood volume. During periods of hypotension, fluids may be administered if the CVP is low or normal. Fluid administration should be slowed or stopped if the CVP begins to rise above normal.

Capillary Refill Time--Place pressure on the oral mucous membranes to produce blanching. The length of time for the normal color to return is the capillary refill time. A delayed refill time indicates arteriolar constriction seen during hypotension or shock.

Oral Mucous Membranes-- Paleness indicates hypotension or shock. Bluishness indicates poor ventilation and low P_{O_2}.

Electrocardiograph (ECG)--Potential cardiac trouble (indicated by arrhythmias and changes in wave form), cardiac arrest, and fibrillation are displayed and may be differentiated on a cardiac monitor (strip chart or oscilloscope).

Respiratory System

Tidal Volume-- May be measured with a ventimeter mounted in the expiratory circuit of the anesthesia machine, an excellent indication of respiratory ventilation. Tidal volumes may be added consecutively so that minute volume is also measured.

Blood Gases--These (P_{O_2} and P_{CO_2}) depend on the interrelationship with the respiratory system, circulatory system, and cellular metabolism.

It is possible to maintain a normal PO_2 and still have the patient deteriorating with a high PCO_2 if ventilation is inadequate to carry off the CO_2. Other blood tests include pH, lactates and pyruvates and their ratio, base excess and equivalent, standard HCO_3, buffer base, and alkali reserve (CO_2 combining power).

Temperature

Temperature may be continually monitored with a rectal thermister. Primates and other small species have a tendency to lose body heat very rapidly under anesthesia. Any animal will lose body heat rapidly during open-chest surgery. Excessive heat loss may be prevented by using a warm-water circulating blanket. Electric heating pads may also be used but must be waterproof to prevent electrical shock (to the patient and the surgeon); these must not be used above the LOW setting for long periods, or severe skin burns may result. A rapid increase in temperature may be the first indication of hyperpyrexia seen in some strains of minipigs and occasionally in dogs.

Urine Output

Urine output indicates renal function and is a good monitor for renal perfusion during shock. Renal shutdown is not common in the dog, but it is in man, primates, and possibly other species.

Electroencephalograph (EEG)

Although routinely used in man, the EEG is difficult to interpret in animals and has not been generally used in veterinary anesthesia.

Eye Position and Pupil Size

Depth of anesthesia with some agents (e.g., halothane) can be monitored by examining the eye.

1. Eye fixed centrally and pupil constricted--light surgical anesthesia.

2. Eye deflected ventrally and pupil not visible--surgical anesthesia.

3. Eye fixed centrally and pupil beginning to dilate--very deep surgical anesthesia and approaching death as pupil continues to dilate.

Pupil dilatation or constriction will be misleading if atropine has been used, but ventral deviation of the eye will still occur.

Reflexes

The stage of anesthesia at which individual reflexes are abolished may vary with the anesthetic agent.

Palpebral Reflex--Closing eyelids in response to medial canthus of the eye being tapped.

Corneal Reflex--Closing eyelids in response to cornea being touched with a wisp of cotton.

Swallowing Reflex--Swallowing in response to jaws being separated and tongue pulled.

Sighing Reflex--Sighing in response to jaws being separated.

Coughing Reflex--Coughing due to upper tracheal or laryngeal irritation.

Patellar Reflex--Extension of the leg in response to the quadriceps tendon being tapped.

Anal Reflex--Constriction of the anal sphincter in response to dilation.

Head-righting--Ability to maintain the head in an upright position without support.

Ear-twitch Reflex--Twitching of the ear in response to breath blown in ear.

Skin Reflex--Pain reaction in response to a needle prick or knife incision.

Tail Waving--Tail is straight and flaccid in the surgically anesthetized monkey and pig.

Pedal Reflex--Flexing the leg in response to toes being squeezed.

Monitoring Anesthesia at USAFSAM

Animals anesthetized for surgery at the Surgical Support Branch, USAFSAM, are monitored and supported during surgery as follows: The electrocardiogram and heart rate are displayed on a cardiac monitor (Electronics for Medicine, Inc.), and arterial blood pressure is measured through a catheter with either a pressure transducer (Statham Instruments) or a mercury manometer. Lactated Ringer's solution or other appropriate fluid is administered through the percutaneous venous catheter that was previously placed for anesthetic induction. This indwelling catheter may also be used for administering emergency drugs if their use becomes necessary. A similar catheter placed in the external jugular vein and advanced into the thorax may be used to measure central venous pressure on a water manometer. Deep-core body temperature is monitored continually with a rectal telethermometer

(Yellow Springs Instrument Co., Inc.). Hypothermia is controlled by a water-circulating pad placed beneath the animal during surgery, and for small primates, by a pediatric incubator in the postoperative recovery phase of anesthesia. Until the animal has recovered his protective reflexes, the anesthetist continuously monitors and periodically records on a specially designed report form (Fig. 10) the animal's vital signs, anesthetic concentrations, fluids, and drugs administered.

ANESTHETIC EMERGENCIES

The period of time from when effective ventilation or circulation stops to the development of irreversible brain damage is usually 4-6 minutes. During these few minutes, death is usually reversible. Clinical death occurs when the first vital system is damaged beyond repair, usually the brain. At this time there will be an absence of the electroencephalogram (EEG) and the pupils will be fixed in dilatation. The primary purpose of resuscitation is to restore effective circulation and ventilation to the vital organs. The keys to success are to have a plan before the situation occurs, be able to make decisions without hesitation, and to have the necessary technics perfected. The following drugs are frequently used in treating anesthetic emergencies.

Epinephrine (41B) is a potent vasopressor, increasing both systolic and pulse pressures. It is also a powerful cardiac stimulant. Cardiac systole is shortened and more powerful, cardiac output increases, and the heart's oxygen consumption and work increase. Ventricular extrasystoles, tachycardia, and fibrillation may be precipitated by the release of endogenous epinephrine when the heart has been sensitized by certain anesthetics such as halothane.

Levarterenol (Norepinephrine) (41B) is predominantly an alpha stimulator and acts to increase systolic, diastolic, and pulse pressure. A marked venoconstriction contributes to an increased vascular resistance. Cardiac output is unchanged or decreased. Levarterenol may produce arrhythmias.

Isoproterenol (Isuprel) (41B) is a powerful beta stimulator which lowers peripheral vascular resistance and increases venous return to the heart. Cardiac output increases due to the chronotropic and inotropic action of isoproterenol on the heart and the increased venous return. Isoproterenol may produce arrhythmias.

Atropine (41B) abolishes many types of reflex vagal cardiac slowing or asystole. Its main cardiovascular effect is cardioacceleration, by blocking vagal effects on the S-A pacemaker.

Lidocaine (41G) is a local anesthetic and is also used to treat ventricular arrhythmias encountered during cardiac surgery or myocardial infarction. When administered intravenously, its antiarrhythmic activity develops rapidly; and it declines quickly when the infusion is discontinued, permitting titration of ventricular ectopic activity. Lidocaine depresses the automaticity of the Purkinje fibers. In anesthetized dogs, doses up to 2-3 mg/kg produce little change in A-V conduction time, contractility, intraventricular conduction, or heart rate. Preparations of lidocaine that contain epinephrine should not be used.

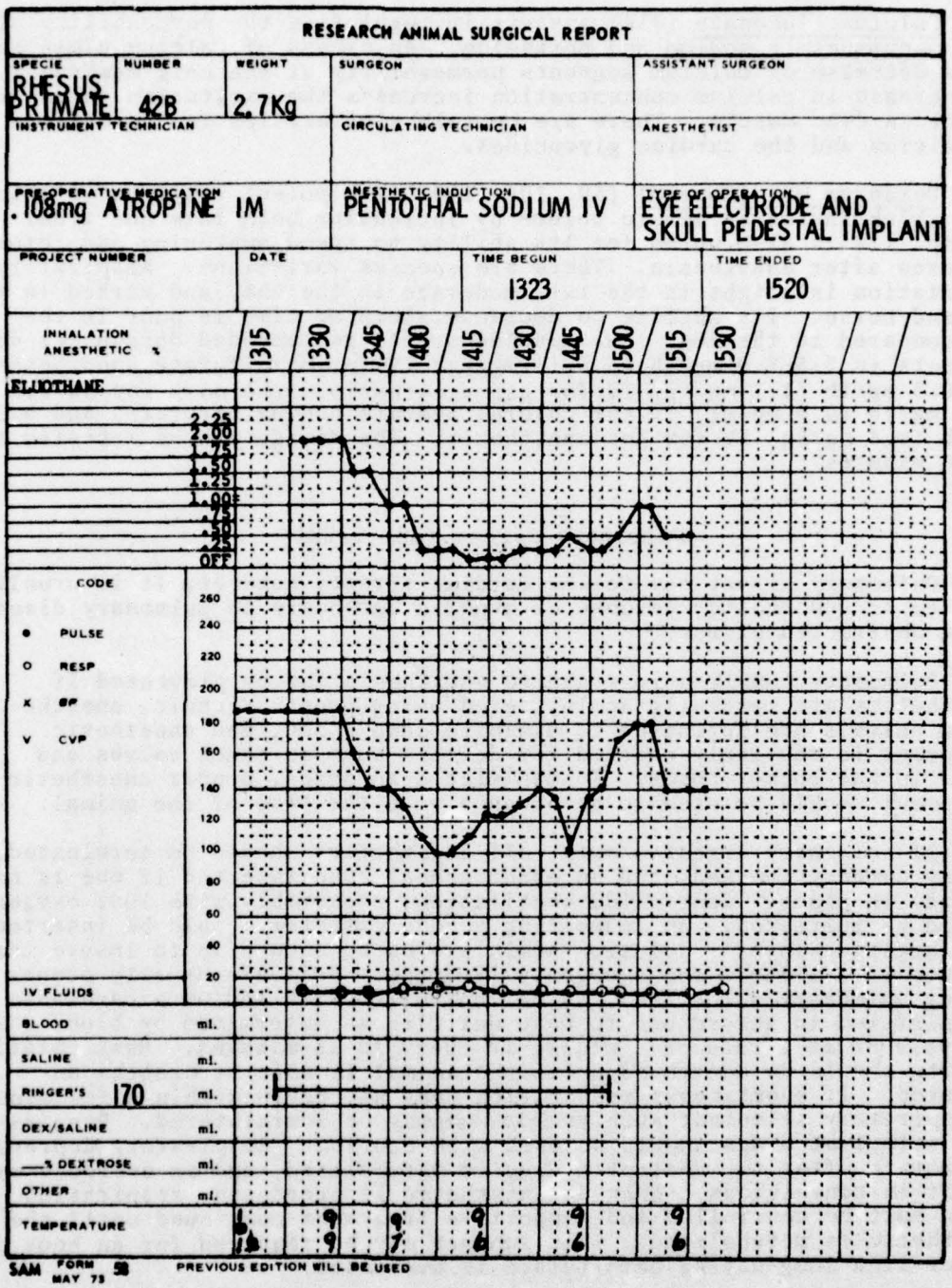

Figure 10. SAM Form 58, Research Animal Surgical Report.

Calcium gluconate (41K) assists in regulating the permeability of cell membranes to sodium and potassium. An excess of calcium diminishes and a decrease of calcium augments permeability of the cell membranes. An increase in calcium concentration increases the excitation threshold of the cardiac muscle. There are certain similarities in the effects of calcium and the cardiac glycocides.

Doxapram HCl (Dopram) (59, 109, 110) is a potent respiratory stimulant which increases minute volume by increasing both rate and tidal volume. It is also noted for its ability to speed awakening and return reflexes after anesthesia. There are species variations. Respiratory stimulation is slight in the rat, moderate in the cat, and marked in the dog and horse. Its ability to decrease sleeping time is poor in the cat compared to the dog. The manufacturer's recommended dosage for dogs and cats is 2.5-5.0 mg/lb (5.5-11 mg/kg) IV for barbiturate anesthesia and 0.5 mg/lb (1.1 mg/kg) IV for gas anesthesia. The dose for horses is 0.25 mg/lb (0.6 mg/kg) IV for chloral hydrate and barbiturates and 0.2 mg/lb (0.4 mg/kg) IV for gas anesthesia. The dosage can be repeated in 15-20 minutes.

Pulmonary Arrest (88, 122K)

Pulmonary arrest may follow cardiac arrest; however, it is usually due to an anesthetic overdose or hypoxia secondary to pulmonary disease or an obstructed airway.

Pulmonary complications due to anesthesia may be prevented if anesthetics are carefully administered using proper technic, anesthetized animals are intubated to minimize dead space, and anesthetic equipment is routinely checked for defects such as stuck valves and leaks in the rubber hoses. To minimize dead space, proper anesthetic equipment should be used in accordance with the size of the animal.

If pulmonary arrest occurs, all anesthetics should be terminated, airway patency checked, and an endotracheal tube inserted if one is not already in place. Controlled ventilation, preferably with 100% oxygen, should be initiated. An indwelling venous catheter should be inserted and lactated Ringer's solution administered by slow drip to insure that a route is available for emergency IV drugs. Acidosis usually occurs during pulmonary arrest and can be controlled with sodium bicarbonate administered in accordance to base deficit, as determined by blood gas analysis or at a rate of 2 meq/kg IV every 10-15 minutes. Resuscitative efforts should be continued until the animal is able to breathe unassisted. If spontaneous respiration does not begin within a few minutes, a respiratory stimulant such as doxapram may be administered. Respiratory stimulant drugs should be used with caution: Respiratory depression may return after the analeptic drug is metabolized, and an overdose may result in convulsions. When an anesthetic is overdosed, respiration often must be controlled and supportive treatment continued until the anesthetic is metabolized. This support may be required for an hour or longer if a long-acting barbiturate is overdosed.

Respiration is often controlled during anesthesia. If the animal is breathing 100% oxygen and is hyperventilated to produce a low P_{CO_2}, the

respiratory drive may be terminated. The ventilation rate may need to be decreased to enable the CO_2 to increase to a level where the respiratory drive will be initiated following the termination of anesthesia. As long as the animal does not become hypoxic, controlled ventilation may be decreased to once every 15-30 seconds until spontaneous ventilation begins.

If respiratory depression is due to narcotics, specific antagonists such as nalorphine 5-10 mg IV or levallorphan 1-2 mg IV, may be administered to effect.

Laryngeal spasms may be controlled by administering a topical anesthetic to the larynx and inserting an endotracheal tube. A muscle relaxant may be needed to facilitate intubation. Meperidine 1-2 mg/kg IV may be administered to decrease tracheal-bronchial irritation.

Cardiac Arrest (73, 80, 88, 93, 94, 97, 122I, 127)

When effective circulation suddenly ceases, cardiac arrest occurs and results in an inadequate supply of oxygenated blood to the vital organs--one of the most important being the brain. The heart also has a high requirement for oxygen. When it fails to receive adequate oxygen, the cells become irritated and fail to conduct the electrical impulses in an efficient, orderly manner; the heart fails to contract and pump blood as it should, which means that the heart's own coronary circulation is impaired. The abnormal electrical impulses of impending cardiac arrest show up as arrhythmias in the EKG. Frequently seen arrhythmias are ectopic ventricular contraction and ventricular tachycardia, which if uncorrected may result in fibrillation or asystole.

When ventricular tachycardia occurs, therapy is directed at maintaining adequate cardiac output and coronary flow. The lungs should be adequately ventilated. Lidocaine hydrochloride is applied topically to the heart or administered intravenously (1-2 mg/kg) at a rate of 1-4 mg/min until the electrocardiogram becomes stable.

Bradycardia is often a sign of impending cardiac arrest. Atropine 0.01 mg/kg IV is effective in countering the vagal influence on heart rate.

Cardiac arrest or fibrillation can be verified by absence of pulse and heart sounds and by the electrocardiogram. If cardiac arrest occurs, the anesthetist should stop all anesthetics and institute 100% O_2 by endotracheal tube and positive pressure ventilation. The cranial end of the animal should be lowered 30% to facilitate venous return, and airway patency should be assured. Cardiac massage should be initiated at a rate of 60-80 times per minute. Arterial blood pressure will indicate the effectiveness of cardiac massage; a systolic pressure of 80 mmHg should be maintained. To counter acidosis, sodium bicarbonate 2 meq/kg is administered intravenously every 10-15 minutes during the resuscitation period. Epinephrine 1:1000 (0.25 to 0.5 cm^3) is administered intravenously or directly into the chamber of the left ventricle to convert the heart from standstill to myocardial activity. If fibrillation occurs, it can be reversed by internal (10-30 watt-second) or external (100 watt-second)

defibrillation. If an electrical defibrillator is not available, drugs such as 2% lidocaine at a dose of 1-2 mg/kg may be administered by the intravenous or intraventricular routes as a bolus, followed by an intravenous drip. Potassium chloride (4%) at a dose of 5 ml may be injected into the ventricle to stop fibrillation; however, depression may be so great that it is difficult to reestablish spontaneous rhythm. Calcium gluconate may be needed to restore cardiac tone. After normal cardiac activity has resumed, 10% calcium gluconate in 5-cm^3 increments can be administered tc stimulate myocardial contraction and improve cardiac output. Isoproterenol, 1 mg in 500 cm^3 of dextrose and saline, is administered in an intravenous drip to stimulate myocardial contraction and venous return.

Shock (104, 122E)

Shock is the clinical syndrome in which the cardiovascular system is not able to adequately perfuse the body organs to sustain their normal function. The origin of shock varies from hemorrhage, heart failure, or neurogenic or endotoxic causes which result in a loss of peripheral vascular resistance. Initially, blood pressure falls. The cardiovascular system tries to maintain blood pressure by vasoconstriction. Capillary shutdown and shunting helps maintain blood pressure; however, tissue perfusion and oxygen utilization decrease. Metabolic acidosis occurs due to anaerobic metabolism. Decreased capillary wall integrity due to toxins results in plasma loss, hemoconcentration, and sludged blood. Vascular collapse and pooling of blood and fluids occur. Poor renal perfusion and renal shutdown contribute to toxin accumulation. When many cells die because of hypoxia, shock becomes irreversible and the animal dies.

Treatment is aimed at establishing an acceptable relationship between the vascular and blood volumes. Both blood pressure and blood flow must be corrected. To correct one and not the other can be disastrous. The following steps are taken in treating shock:

1. Circulating blood volume should be maintained. Whole blood is administered if the PCV is below 30%; blood expanders such as dextran, plasma, or 5% dextrose in saline, are infused if the PCV is elevated.

2. High viscosity and sludging of the blood can be controlled by low-molecular-weight dextran (2-10 cm^3/lb, or 4-22 cm^3/kg) repeated every 30 minutes until the PCV is 40%-50%; 0.5 mg/lb (1.1 mg/kg) heparin IV may also be administered.

3. Ischemia of the microcirculation, venous spasm, and decreased venous return are treated with the adrenergic blocking agents Dibenzyline 0.25-1.0 mg/lb (0.55-2.2 mg/kg) in 500 cm^3 glucose administered over 1 to 2 hours or chlorpromazine HCl 0.1-0.3 mg/lb (0.22-0.66 mg/kg) IV or the Beta adrenergic stimulator isoproterenol 1 mg in 500 cm^3 glucose IV to effect.

4. Vasopressors should be used only to maintain acceptable blood pressure. Elevated blood pressure without concurrent microcirculation

is of little value. Epinephrine 0.1%, 1 cm^3 diluted to 100 cm^3, is titrated one drop at a time, or 1 ml of 0.2% norepinephrine in 250 cm^3 5% dextrose is administered 2-10 drops at a time, until blood pressure returns to above 80 mmHg.

5. Corticosteroids and antihistamines are administered to prevent cellular injury and control histamine release. Hydrocortisone succinate 2-10 mg/lb (4-22 mg/kg) IV per hour. Diphenhydramine HCl 0.5-1.0 mg/lb (1-2 mg/kg) IV per hour, repeated as needed.

6. Intravenous antibiotics are administered to prevent bacterial proliferation. Crystalline potassium penicillin G 50,000 units and 1 g streptomycin in 500 cm^3 saline is administered at a rate of 10-20 ml/lb (22-46 ml/kg) as a continuous drip. It may be repeated every 6 hours.

7. Sodium bicarbonate 2 meq/kg IV is administered to counter acidosis. It may be repeated every 15-30 minutes.

8. If the arterial P_{O_2} decreases below 70 mmHg, the animal should be intubated and ventilation assisted with 40%-100% oxygen, or the animal may be placed in an intensive-care cage in which the oxygen content and temperature can be controlled.

9. Body temperature should not be allowed to decrease below 94°F (35°C). Temperature may be maintained with water-circulating heating pads.

ANESTHETIZING DOGS

Preanesthetics

Anticholinergics--

1. Atropine sulfate 0.04 mg/kg IM or subQ (122).

2. Scopolamine 0.01-0.02 mg/kg (2, 122).

Tranquilizers--

1. Chlorpromazine HCl (Thorazine) 0.5 mg/lb (1.1 mg/kg) IV, 1 mg/lb (2.2 mg/kg) IM, 1.5 mg/lb (3.3 mg/kg) per os (69).

2. Promazine HCl (Sparine) 1.3 mg/lb (2.9 mg/kg) IV (69).

3. Triflupromazine HCl (Vetame) 0.5-1 mg/lb (1.1-2.2 mg/kg) IV, 1-2 mg/lb (2.2-4.4 mg/kg) IM (69).

4. Acetylpromazine maleate (Acepromazine) 0.25-0.5 mg/lb (0.55-1.1 mg/kg) IV, IM, or subQ (69).

5. Xylazine (Rompun): Xylazine is an adrenergic-cholinergic neuron inhibitor with sedation, analgesia, and muscle-relaxation properties. Dosage levels vary between 0.5 and 2 mg/lb (1.1-4.4 mg/kg).

Analgesic effects last 15-30 minutes, followed by sedative effects lasting up to 3 hours. Barbiturate anesthesia can be reduced 75% following IV xylazine and 30%-50% following IM xylazine. Supplemental anesthesia has to be administered to enable intubation of dogs. Xylazine decreases respiratory and heart rates and produces a transitory drop in blood pressure (90). It has been used successfully for cesarean sections, supplemented with 2% lidocaine at the incision site, without adverse effects to the puppies. Fifteen minutes after administration, dogs are able to walk even though they are in a drowsy resting state (144). Increased doses do not increase the depth of sedation but do increase the duration of effect. It is recommended that atropine be administered prior to xylazine (2, 122).

6. Triflupromazine: A number of anesthetics, narcotics, and tranquilizers were analyzed for their effects on the transit time of barium in the gastrointestinal system. Triflupromazine hydrochloride 0.5 mg/lb (1.1 mg/kg) IV, followed by a 15-min period before administration of barium, produced predictable effects and decreased stomach and intestinal motility to a speed that enabled radiographic examination. Restraint was adequate for 3 hours (145).

Narcotics--

1. Morphine sulfate: Effects (sedation or excitement) are species and dose related. Depression and analgesia occur at the lower therapeutic doses. Strychnine-like convulsions and death may occur at the higher doses. A dose of 0.5-0.75 mg/kg is adequate for premedication. Sedative aspects are miosis, respiratory depression, bradycardia, hypothermia, and reduced response to external stimuli. The excitement aspects are mydriasis, nausea, panting, and convulsions (122).

2. Meperidine (Demerol): Premedication 2.5-6.5 mg/kg; postoperative analgesia 5-10 mg/kg (122).

3. Methadone hydrochloride 0.1-0.5 mg/kg (122).

4. Apomorphine sulfate 0.1 grain (6.5 mg) subQ/dog (2, 122).

5. Pentazocine (Talwin) 1.5-3 mg/kg. High doses of 6-10 mg/kg can produce tremors and convulsions (122). Pentazocine (3.3 mg/kg IM) was compared with meperidine (5.5 mg/kg IM) and morphine in the dog (111). Pentazocine increased the tidal volume and produced a transitory 18% decrease in blood pressure, compared to a decreased tidal volume and a 75% and 25% decrease in blood pressure for meperidine and morphine respectively. Meperidine was considered more effective for controlling pain after surgery of the extremities and thorax. For both pentazocine and meperidine, the dogs tended to relax and sleep. The advantages of pentazocine are that it is not subject to narcotic controls and it does not decrease the tidal volume or blood pressure to the degree seen with meperidine and morphine.

6. Innovar-Vet: Produces sedation, immobilization, adrenergic blockade, bradycardia, and decreased blood pressure. When used as a preanesthetic for major surgical procedures, Innovar-Vet is administered

at a dose of 1 ml/40 lb (18 kg) IM, followed in 10 minutes with an IV barbiturate; or 1 ml/25-60 lbs (11-27 kg) IV, followed in 15 seconds with an IV barbiturate. When used alone the dose is 1 ml/20 lb (9 kg) IM or 1 ml/25-60 lbs (11-27 kg) IV. Innovar-Vet may be used in combination with a local anesthetic for major surgical procedures such as cesarean section. Atropine sulfate should be administered to prevent defecation, salivation, and bradycardia.

Narcotic Antagonists--

1. Nalorphine HCl (Nalline) 5-20 mg IV.

2. Levallorphan tartrate (Lorphan) 0.5-2 mg IV.

Neuromuscular Blockers--

1. Succinylcholine 0.3 mg/kg produces paralysis for 5-10 minutes (122J).

2. D-tubocurarine 0.4 mg/kg. The effects may be reversed with atropine sulfate, to counter the muscarinic effects of neostigmine, followed with neostigmine in a 0.05% solution at a dose of 0.5 to 1 ml IV (122J).

3. Gallamine 1 mg/kg produces complete paralysis for 15-20 minutes. Gallamine may be reversed with neostigmine (122J). Gallamine is excreted unchanged in the urine and, therefore, is contraindicated in renal failure.

Inhalation Anesthesia

Halothane and methoxyflurane are the inhalation anesthetics most frequently used in the canine. The technics described on page 49 are routinely used to administer halothane anesthesia to canines at USAFSAM.

The effects of halothane and halothane-nitrous oxide (N_2O) anesthesia in the dog with controlled and spontaneous ventilation have been studied (125, 126). Halothane is a dose-dependent cardiopulmonary depressant. With controlled ventilation, adding 75% N_2O did not alter the circulatory depression seen with halothane alone. With spontaneous ventilation, there was no difference between the circulatory depression of halothane versus halothane plus 25% N_2O; but with halothane plus 75% N_2O, a significant increase in cardiovascular performance was observed. The reason for an increased sympathetic response and improved cardiovascular performance was not determined; however, it was postulated that it was due to the undesirable effects of inefficient spontaneous respiration and resultant hypercapnia, hypoxemia, and acidosis rather than a beneficial effect from N_2O.

Halothane may increase the sensitivity of the heart to the arrhythmic actions of adrenergic agents (epinephrine, norepinephrine, metaraminol, deoxyepinephrine, adrenalone, nordefrin, and dopamine. Thiobarbiturates (thiamylal sodium and thiopental sodium) used for

anesthetic induction frequently produce arrhythmias. Dogs that were pretreated with chlorpromazine hydrochloride (2 mg/kg IV), acetylpromazine maleate (1 mg/kg IV), or propranolol (1 mg/kg IV) were protected against the arrhythmic effects (fibrillation) of epinephrine, halothane, and thiobarbiturate combinations (141).

Postoperative renal dysfunction may occur in man following methoxyflurane anesthesia. Renal studies in dogs have shown that renal dysfunction apparently does not occur during acute exposure of methoxyflurane (84).

Injection Anesthesia

Barbiturates--

1. Pentobarbital sodium (Nembutal) 13 mg/lb (28.6 mg/kg) IV. Duration of surgical anesthesia from the initial dose averages 30 minutes. Complete recovery occurs in 6-18 hours (69).

2. Thiopental sodium (Pentothal) 20-30 mg/kg (69).

3. Thiamylal sodium (Surital) 17.5 mg/kg IV produces surgical anesthesia lasting approximately 15 minutes (69).

The technics described on page 32 are used to administer intravenous barbiturates.

Dissociative Agents--

1. Ketamine anesthesia was used in 327 dogs representing 35 breeds. The dogs were given 0.02 mg/lb (0.04 mg/kg) atropine sulfate and 0.25 mg/lb (0.55 mg/kg) Acepromazine, followed in 10-15 minutes with ketamine 5-10 mg/lb (11-22 mg/kg) IM. Dogs less than 20 lbs (9 kg) received 10 mg/lb (22 mg/kg) ketamine, while larger dogs received 7 mg/lb (15 mg/kg) for major procedures and 5 mg/lb (11 mg/kg) for minor procedures. For major surgical procedures the dogs were given thiamylal sodium 5 minutes after administration of ketamine. The amount of thiamylal required was usually less than 25% of the normal dose. Adverse effects were tonic-clonic convulsions in 3.4% of the dogs within 2-7 minutes after the ketamine was administered. Thiamylal sodium alleviated these seizures. Salivation was not controlled by the normal dosage of atropine 0.02 mg/lb (0.04 mg/kg) (55).

2. CI-744 5.5-9 mg/kg IM was satisfactory for anesthesia. Induction averaged 7 minutes; sleeping time, 42 minutes; and total immobilization, 126 minutes. Cardiovascular effects were slight at 5.5 mg/kg IM. Tachycardia was consistent. Blood pressure and cardiac output changes were variable. Pa_{O_2} decreased, P_{CO_2} increased, and pH change was usually slight (134).

ANESTHETIZING CATS

Preanesthetics

Anticholinergics--Atropine sulfate 0.04 mg/kg subQ.

Tranquilizers--

1. Chlorpromazine HCl (Thorazine) 0.5 mg/lb (1.1 mg/kg) IV, 1 mg/lb (2.2 mg/kg) IM, 1.5 mg/lb (3.3 mg/kg) per os (69).

2. Triflupromazine HCl (Vetame) 2-4 mg IM (69).

3. Acetylpromazine maleate (Acepromazine) 0.5-1 mg/lb (1.1-2.2 mg/kg) IV, IM, or subQ (69).

4. Xylazine (Rompun) 0.5-1 mg/lb (1.1-2.2 mg/kg) IM or subQ. Xylazine possesses a wide margin of safety. Increased doses do not increase the depth of sedation but do increase the duration of effect. Atropine should be administered prior to xylazine (69). Xylazine 0.5 mg/lb (1.1 mg/kg) may be used as a preanesthetic emetic in cats, much as morphine is used in the dog. Subsequent sedation lasts 30-90 minutes. Analgesic effects are not observed at this dosage (4).

Narcotics--

1. Meperidine (Demerol). Sedation is poor in the cat. Analgesic properties have not been evaluated. The dose should not exceed 11 mg/kg subQ or IM. Meperidine alone or in combination with a tranquilizer potentiates general anesthetics; therefore, even though the cat does not appear depressed, the anesthetic and lethal doses of general anesthetics are lowered (2, 122).

2. Morphine 0.1 mg/kg has been administered to cats if a tranquilizer such as promazine 2 mg/kg was given simultaneously to depress the excitatory effects. The standard dose of 0.5 mg/kg for the dog may produce restlessness and convulsions in the cat (2, 122).

Morphine 0.1-0.5 mg/kg and meperidine 2.5-5 mg/kg have been tolerated in the cat. Dosages above these produced salivation, agitation, mydriasis, and vocalization. Respiratory depression was pronounced at dosages above 0.5 mg/kg morphine and 5 mg/kg meperidine. Preanesthetic meperidine or morphine in the cat is probably of no value in ketamine anesthesia (49).

Neuromuscular Blockers--

1. Succinylcholine 1 mg/kg produces paralysis for 2-3 minutes (122).

2. D-tubocurarine 0.3 mg/kg is a paralyzing dose (69).

3. Gallamine triethiodide (Flaxedil) 1 mg/kg produces complete paralysis for 10-20 minutes (69, 122J).

Inhalation Anesthesia

Animals which usually weigh less than 7 kg, such as cats, should not be anesthetized by circle systems because of respiratory resistance, carbon dioxide accumulation, and respiratory acidosis. Nonrebreathing systems such as the Ayres T-piece are recommended. Cats are induced with thiamylal sodium or thiopental sodium or by face mask with 2 liters/min 1:1 oxygen/nitrous oxide plus 4%-5% halothane. The cat is then intubated with a 16-18 French neonatal endotracheal tube and maintained on the halothane mixture. Atropine (1/320 grain subQ) is the only preanesthetic used. The phenothiazine tranquilizers are alpha blockers, narcotics are respiratory depressants, and ketamine masks normal reflexes to evaluate anesthesia; therefore, these preanesthetics are not used (102).

In newborn kittens, methoxyflurane was satisfactory for induction and maintenance of anesthesia. A 2-ml plastic syringe case was used as a face mask. Atropine 0.06 mg/kg was administered prior to induction. The barbiturates pentobarbital and thiamylal and inhalation anesthetic ether were considered unsatisfactory (115).

Halothane inhalation anesthesia is administered at USAFSAM by the technics described on page 49.

Injection Anesthesia

Ketamine (CI-581)--Young and hyperexcitable cats may require higher dosages, and very old cats a smaller dose. Induction time, depth and duration of anesthesia, and recovery time are dose related. In one study, induction time was 3 minutes or less. Doses below 22 mg/kg IM produced chemical restraint, and 25-44 mg/kg produced cataleptoid anesthesia lasting 20-40 minutes--adequate for short surgical procedures. Complete recovery required 6-7.5 hours. Cardiac output and systolic blood pressure were increased. Mild respiratory depression, tachycardia, and clonic muscle spasms were adverse side effects in a small percentage of cats. When ketamine was used for surgical anesthesia, alone or supplemented with a volatile anesthetic, the body temperature decreased as much as 8°F (4.4°C). Recovery stress was reduced when the cat was placed in a warm, dark, quiet recovery area. Body temperature should be monitored and supplemental heat provided. If clonic spasms or mild convulsions occur during recovery, they may be controlled with one-sixth to one-fourth the normal dose of sodium thiamylal. Ketamine is excreted primarily through the urine and should not be used if there is urinary tract obstruction (urolithiasis) or renal impairment (6).

When xylazine was used as a preanesthetic before administering ketamine, muscle stiffness has been eliminated and the cat remained sedated through the recovery period. A dose of 0.5 mg/lb (1.1 mg/kg) IM xylazine followed in 20 minutes with 7-10 mg/lb (15-22 mg/kg) IM ketamine produced 30 minutes of analgesia and relaxation with a quiet, uneventful recovery period. Xylazine produces vomiting 3-5 minutes after administration. Maintenance doses of ketamine may be administered to prolong anesthesia without overriding the relaxation effects of xylazine (3, 4).

Tiletamine (CI-634)--Tiletamine, a phencyclidine derivative, administered at a rate of 11 mg/kg IM produces immobilization within 2-3 minutes. Righting reflexes return within 2 hours. Cardiovascular changes (blood pressure, heart rate) are not significant, but an irregular breath-holding pattern of respiration develops. Respiratory depression produces respiratory acidosis and decreased oxygen tension. After IV injection of tiletamine, arrhythmias are common. Blood pressure and heart rate consistently increase (17).

CI-744--Satisfactory anesthesia for abdominal surgery is obtained with doses of 6-16 mg/kg IM. Induction time averages 5.5 minutes, with anesthesia lasting approximately 60 minutes. Ambulation occurs 2 hours following anesthesia. Relaxation is adequate for surgery, and recovery is smooth. CI-744 is free of the undesirable side effects of ketamine in cats (134).

Barbiturates--Pentobarbital sodium 13 mg/lb (28.6 mg/kg) IV produces surgical anesthesia lasting 30 minutes. Recovery is complete in 6-18 hours. The dose for thiopental sodium is 20-30 mg/kg IV (122). Intravenous anesthetics are administered at USAFSAM by the technics described on page 32.

ANESTHETIZING SHEEP AND GOATS

Sheep and goats do not have the regurgitation and salivation problems that cattle have.

Preanesthetics

Anticholinergics--Atropine sulfate 15 mg/50 lb (22.5 kg) prior to anesthesia, with 3-6 mg every 15 minutes thereafter (69).

Tranquilizers (69)--

1. Chlorpromazine HCl (Thorazine) 0.5 mg/lb (1.1 mg/kg) IV, 1 mg/lb (2.2 mg/kg) IM or per os.

2. Triflupromazine HCL (Vetame) 0.5 mg/lb (1.1 mg/kg) IV.

3. Diazepam (Valium) 0.25-0.5 mg/lb (0.55-1.1 mg/kg).

Neuromuscular blockers--Succinylcholine 0.02 mg/kg produces paralysis for 6-8 minutes.

Inhalation Anesthesia

Anesthesia equipment used for large dogs can be used for sheep and goats. Induction may be attained by the intravenous administration of short-acting thiobarbiturates or by inhalation anesthesia induction via a face mask. Halothane is the inhalation anesthetic of choice because of its ease of induction, potency, and rapid recovery period (122F).

Halothane provides complete relaxation of the uterus and has been used successfully for uterine surgical procedures in standard-sized

and pygmy female goats. Premedication was atropine sulfate 2-6 ml of a 0.4 mg/ml solution administered IV. Induction was with 4% thiamylal sodium at a dose of 0.34-0.44 ml/kg IV. Following intubation, the animals were maintained on halothane (29).

Injection Anesthesia

The jugular or cephalic vein may be used for intravenous injections. Thiopental sodium and pentobarbital sodium are safe for short procedures and induction prior to inhalation anesthesia. A 2.5%-5% solution is used for small sheep and goats, and a 10% solution for large adults. The dose is 30-40 mg/kg IV titrated to effect (122F).

CI-744, the combination of a cataleptoid anesthetic (tiletamine HCl) and nonphenothiazine tranquilizer (Zolazepan) in a 1:1 ratio, dissolved in sterile distilled water at a concentration of 20%, has been used to anesthetize sheep. The initial dose of CI-744 was 8-16 mg/kg IV (jugular vein) by rapid injection. Induction was smooth and rapid (15-30 sec). Surgical anesthesia was attained within 0.5-4.8 minutes and ranged from 0.8 to 3.7 hours. To prolong surgical anesthesia, maintenance doses up to 50% of the original dose were administered IV or IM. Following surgical anesthesia, the sheep were able to stand within an average of 42 minutes (22).

CI-744 10-20 mg/kg IV has provided satisfactory anesthesia, lasting 40 minutes, for neurosurgical procedures in sheep. Repetitive injections prolonged anesthesia without adverse effects. Following surgical anesthesia there was an extended period of chemical restraint lasting from 25-40 minutes. Bloating did not occur since the sheep continued to eructate while anesthetized (134).

Sheep were anesthetized with atropine sulfate 0.2 mg/kg IM, followed in 15 minutes with acetylpromazine 0.55 mg/kg IV and 10 minutes later with ketamine 22 mg/kg IV or IM. For splenectomies, surgical anesthesia was maintained from 1 to 1.5 hours by intermittent administration of ketamine 2-4 mg/kg IV. Immobilization was rapid following the ketamine administration. The preanesthetics controlled salivation and increased muscle relaxation. To prevent apnea, IV ketamine should be administered slowly over a period of 45-60 seconds. Limb movement, open eyes, and nystagmus are normal with ketamine and are not associated with painful stimuli (132).

ANESTHETIZING CATTLE

Complications due to anatomy and physiology may be encountered in cattle under general anesthesia. Respiratory embarrassment due to intra-abdominal pressure on the diaphragm may occur when cattle are placed in lateral recumbency. Innertubes can be used for padding to decrease such pressure. Rumenal tympany and regurgitation are controlled by withholding food for 18 hours and water for 6 hours. An endotracheal tube should be inserted to prevent inhalation of ingesta, and the head lowered to enable saliva to flow from the mouth. It is difficult to suppress salivation in cattle with drugs (122F).

Preanesthetics

Anticholinergics--Atropine sulfate 0.2 mg/100 lb (45 kg). It is of limited value in large ruminants (69, 122).

Tranquilizers--

1. Chlorpromazine HCl 1 mg/kg IM as a preanesthetic or 1.5 mg/kg IM when used alone. Maximum effect occurs within 30-60 minutes. Cattle are unable to rise for 1-2 hours. Chlorpromazine is more effective than promazine or trimeprazine in cattle (122F).

2. Promazine HCl 0.5 mg/lb (1.1 mg/kg) IV (69).

3. Triflupromazine (Vetame) 5 mg/100 lb (45 kg) IV (69).

4. Diazepam (Valium) 0.25-0.5 mg/lb (0.55-1.1 mg/kg) (69).

Neuromuscular Blocking Agents--

1. Succinylcholine 0.02 mg/kg produces paralysis for 6-8 minutes (122F).

2. D-tubocurarine 0.05 mg/kg is safe in young cattle. Very small doses, however, often produce death in adult cattle (122F).

3. Gallamine 0.4 mg/kg is effective for calves; however, prolonged apnea may be produced. Adult cattle experience respiratory difficulty at doses above 1.5 mg/kg (122F).

Basal Narcosis--Chloralhydrate in a 10% solution is administered at a dose of 10-12 g/100 kg IV to produce hypnosis and sedation to facilitate restraint and casting. To decrease undue excitement, range cattle and bulls should be tranquilized before chloral hydrate is administered. Chloral hydrate in doses sufficient for surgical anesthesia is dangerous; it should be used only as a sedative (122F).

Inhalation Anesthesia

Induction is usually with intravenous barbiturates. Large animal inhalation equipment is needed for adult cattle. Calves up to 5 months old may be maintained on equipment suitable for large dogs. Halothane is the inhalation anesthetic of choice because of its potency and safety (122F).

Calves, 2-4 weeks old and weighing 47.7-61.4 kg, present special anesthesia and ventilation problems when subjected to cardiovascular surgery and cardiopulmonary bypass. In one study (30), the calves were premedicated with 8 mg atropine sulfate IM 30 minutes before anesthetic induction with halothane-N_2O-O_2 administered through a facial mask. Calves were then intubated and maintained on inhalation halothane anesthesia. Moderate to severe respiratory acidosis occurred in calves that were allowed to breathe spontaneously before thoracotomy. Large tidal volume and high-pressure (30 cm H_2O) controlled ventilation was required to prevent hypoxia; however, undesirable hypocapnia and

metabolic acidosis were side effects. Small tidal volume and low-pressure ventilation resulted in hypoxia, hypercapnia, and atelectasis. Calf lungs are composed of thick pleura and extensive supportive tissue. Other factors which contribute to the requirement for high ventilation pressures are positioning during surgery, small amounts of surfactant, and pressure from abdominal viscera. Additional problems concerning anesthetic maintenance, extracorporeal circulation, cardiac surgery, and the postoperative care of calves undergoing cardiac surgery have been discussed in detail (108).

Intravenous Anesthesia

Barbiturates are used for induction prior to inhalation anesthesia or for short procedures, but are not recommended for long procedures because of prolonged recovery periods. Calves below 4 months of age have difficulty in eliminating barbiturates and may experience prolonged anesthesia lasting 2-3 days. Intravenous anesthetics are administered in the jugular vein. Thiopental sodium and pentobarbital sodium are frequently used. The dose for each is 1 g/100 kg. Each gram is dissolved in 5 ml of solution to enable the total dose for a 400-kg animal to be administered via a 20-cm^3 syringe (122F).

ANESTHETIZING SWINE

Pigs are considered poor anesthetic risks. Borderline water intake and increased excretion of fluids due to stress may precipitate salt poisoning. Because of the anatomy of the larynx and soft palate, pigs under deep anesthesia and not intubated suffer from respiratory embarrassment. The pig heart is smaller in proportion to body size than is the heart of other domestic animals, and the small heart size may be a disadvantage during periods of anesthetic stress (24).

Preanesthetics

Anticholinergics--Atropine sulfate 0.04 mg/kg.

Muscle Relaxants--

1. Succinylcholine chloride 2.2 mg/kg produces paralysis lasting 2-3 minutes (122J). The minimum dose to produce neuromuscular block is 0.4 mg/kg (69).

2. D-tubocurarine 0.25 mg/kg IV (122J).

3. Gallamine triethiodide 2 mg/kg (122J).

Tranquilizers--

1. Triflupromazine HCl 40 mg/100 lb (45 kg) IV, 60 mg/100 lb (45 kg) IM (69).

2. Diazepam 0.25-0.5 mg/lb (0.55-1.1 mg/kg) (69).

Anesthetic Technics

Pigs are difficult to anesthetize because their size and temperament make them hard to restrain, superficial veins are often not readily available, and laryngospasm can complicate intubation. Several different agents are administered as sedatives for restraint, muscle relaxants for intubation, and inhalation agents for anesthesia. It is easier, therefore, to discuss the complete anesthetic regimens that different investigators have used rather than discussing each anesthetic agent independent of one another.

Pentobarbital sodium 22 mg/kg IV has been administered through the subcutaneous abdominal vein (cranial superficial epigastric vein) (120). A dose of 10-30 mg/kg IV has provided anesthesia for 15-45 minutes (69).

The optimum dose of 10% thiamylal sodium was considered to be 2 ml/100 lb (45 kg) up to 400 lb (180 kg) and 0.5 ml for each 100 lb above 400 lb, up to a maximum of 10 ml administered through the marginal ear vein (86). A dose range of 10-20 mg/kg thiamylal sodium has also been recommended (69).

Methods for anesthetizing pigs for heart-lung bypass have been investigated (96). The following technics for induction were evaluated:

1. Thiamylal sodium 10% injected into the marginal ear vein at a dose of 12-18 mg/kg. Pigs were intubated and administered 2.5%-3% halothane for induction which was reduced to 0.75%-1% for maintenance. Pigs were often difficult to intubate due to laryngospasm.

2. Succinylcholine chloride 1 mg/kg IM provided relaxation. A canine face mask was used to administer oxygen. After 1-2 minutes the pigs were intubated and maintained on halothane. Succinylcholine provided consistent relaxation and immobilization.

3. Fentanyl 0.4 mg and droperidol 20 mg/14 kg IM plus atropine sulfate 1 mg/20 kg were administered as preanesthetics. Following tranquilization, 4% halothane was administered through a canine face mask. The pigs were intubated and maintained on 0.5%-1.5% halothane. The addition of 50% nitrous oxide decreased induction time by half and reduced the amount of halothane used prior to intubation. This was the technic of choice for induction.

During cardiopulmonary bypass, volatile anesthetics could not be used because of pulmonary artery occlusion. Anesthesia was maintained by titrating 10% thiamylal into the reservoir of the oxygenator. A second technic utilized 0.3 mg/kg d-tubocurarine chloride, followed with 0.5 mg fentanyl and 12.5 mg droperidol in 100 ml of saline administered as an IV infusion in a 1-hour period. After the first hour, anesthesia was maintained with IV infusion of 0.5 mg fentanyl in 500 ml saline at a rate of 0.1 mg/hr. Fentanyl administered at a rate faster than 0.1-0.2 mg/hour produced hypotension. Atropine 1 mg/20 kg had to be administered every 2 hours to prevent bradycardia. Fentanyl-droperidol anesthesia was considered superior to thiamylal-halothane anesthesia, which produced a marked negative effect on myocardial contractivity and increased peripheral vascular resistance. The potent analgesic effect of fentanyl was considered advantageous during the recovery period.

Three of six pigs died in ventricular fibrillation 30-60 minutes after being removed from positive pressure ventilation where they had been ventilated 20 cycles/min, +25 and -6 cm H_2O. This technic resulted in respiratory alkalosis and lowered arterial pressure. Problems of fibrillation due to ventilation were eliminated when arterial PCO_2 and pH were maintained at normal values using a rate of 12/min at pressures of +15 and -6 cm H_2O (96).

Pigs have been premedicated with 30 mg/lb (66 mg/kg) Innovar-Vet and 0.4 mg/lb (0.88 mg/kg) atropine sulfate; 20 minutes later, halothane was administered through a face mask. When a light plane of anesthesia was achieved, 0.5 mg/lb (1.1 mg/kg) IV succinylcholine chloride was administered in the marginal ear vein and the pig was intubated. Respiration was controlled for 5-6 minutes until spontaneous respiration resumed. The anatomy of the pig larynx and pharynx and the technic used by the authors to intubate pigs were described in detail (27).

Succinylcholine 0.88-1.1 mg/kg IV administered through a 25-ga needle in the marginal ear vein has resulted in muscle relaxation and cessation of spontaneous ventilation for 4-7 minutes. An endotracheal tube and esophageal stethoscope were passed, and the animal was anesthetized with halothane during the period of muscle relaxation (28).

Forty sows weighing 140-473 kg were premedicated with 2.5 mg atropine sulfate subQ, followed with 1.5-2 mg/kg phencyclidine HCl. The sows became recumbent within 5 minutes. A mask was used to administer an initial concentration of 7% halothane in a 3:2 H_2O-O_2 gas mixture. Halothane was reduced to 1.5%-2.5% for maintenance. Concentrations as high as 10%-12% halothane were administered for short periods to provide sufficient relaxation for intubation (130).

The greatest difference between doses of phencyclidine in the pig is duration of effect. In one study (129) the average time for the normal gait to be restored was 2 hours at 1 mg/kg, 3 hours at 2 mg/kg, and 24 hours at 8 mg/kg. There was a high degree of individual variation. The optimum dose rate for the production of sedation with complete ataxia and no evident toxicity appeared to be 2 mg/kg. In some heavy animals over 125 kg, a dose of 2 mg/kg was not sufficient to produce recumbency. Half the original dose was repeated 10 minutes after the first injection to achieve recumbency.

Ketamine was evaluated in swine as an anesthetic and immobilizing agent. As the sole anesthetic agent, ketamine 20 mg/kg IM was adequate for short surgical procedures lasting 10-20 minutes. Prolonged surgery required supplementation with either 2% lidocaine by local infiltration, thiopental sodium 6.6-11 mg/kg IV, ketamine-thiopental sodium combination followed by 2% halothane in oxygen via endotracheal tube, or 2% halothane via face mask. Atropine sulfate 0.04 mg/kg IM was administered to control salivation. Excitement frequently occurred during the recovery period in animals that were not supplemented with thiopental sodium or halothane. Two boars that received ketamine died during the recovery period. Ketamine in swine appears to offer its greatest advantage as an immobilizing agent (131).

Pigs weighing between 50-100 kg were anesthetized with ketamine 15 mg/kg IM for induction, followed by suxamethonium (succinylcholine)

1 mg/kg IV in the lateral ear vein to facilitate endotracheal intubation. Maintenance anesthesia was with nitrous oxide-oxygen 3:1 liters/min plus supplemental barbiturate as required. Further relaxation was achieved with gallamine or tubocurarine. Gallamine triethiodide 120 mg was administered as soon as respiration recommenced, and was supplemented with 80-120 mg as required (average dose 0.07 mg/kg per hour). The adult human doses of neostigmine and atropine counteracted both gellamine and tubocurarine. Gallamine 720 mg administered over a 90-min period could be reversed with 0.6 mg atropine and 1.25 mg neostigmine (101).

Malignant hyperthermia has been triggered in swine (Poland China, Landrace, Pietrain) by halothane, chloroform, succinylcholine Cl, and stress, but not by thiopental or nitrous oxide. Early blood changes include hypercapnia, acidosis, high inorganic phosphate, and excess lactic acid. Clinical signs began with tachycardia, hyperventilation, rigidity, and blotchy skin cyanosis, and progressed to hyperthermia (average 110°F) (43°C), cardiac arrhythmia, bradycardia, and death (53).

At USAFSAM we use 2.5% pentothal sodium (10 mg/kg IV) administered through the lateral ear vein or venous sinus located at the medial canthus of the eye. The barbiturate anesthesia is titrated to produce light anesthesia. Halothane at a 4% concentration is administered by means of a face mask until relaxation is sufficient to enable endotracheal intubation by the technic described on page 30. Anesthesia is maintained with 1%-2% halothane. Pentothal is our anesthetic of choice for induction. Induction is quick and its effects are not present when the halothane anesthesia is terminated. We have used a mixture of 1.5 mg Acepromazine, 4 mg Demerol, and 0.04 mg atropine per kg IM as a preanesthetic. With this preanesthetic the swine do not become sedated before 15-20 minutes and still often resist manual restraint. Phencyclidine administered as a preanesthetic at a dose of 6 mg/kg IM has been recommended by one author to provide at least 2 hours of anesthesia under which swine could be intubated (95). We were not able to intubate swine with phencyclidine without supplemental halothane to relieve the laryngospasm. Thirty miniature swine received 6 mg/kg phencyclidine and 0.4 mg/kg atropine sulfate and were maintained on halothane for 10-15 minutes to enable muscle relaxation sufficient to obtain baseline electrocardiograms. Two of these pigs remained recumbent for 24-36 hours before dying. Pigs anesthetized for cardiac bioinstrumentation with phencyclidine and halothane had prolonged recovery periods compared to pigs anesthetized with a pentothal-halothane combination.

ANESTHETIZING HORSES

Difficulties in handling and managing horses are primarily due to their size and weight. Nervous and highly excitable animals may injure themselves and their handlers. Special precautions are needed to prevent injury when a horse falls following administration of an anesthetic and struggles during recovery (122D).

Anesthetic complications in the horse usually involve the respiratory and cardiovascular systems and occur most frequently during induction, the early phases of maintenance, and recovery. Recognition and treatment of the most frequently encountered anesthetic complications in the horse have been described (113).

Preanesthetics

Anticholinergics--Atropine sulfate 0.04 mg/kg subQ or IM (112), or up to 65 mg (122D), may be administered 20 minutes before anesthesia.

Narcotics--

1. Meperidine HCl 0.5 mg/kg IM is administered 45 minutes before anesthetic induction. It may be administered by the IV route during or immediately following surgery for analgesia. Doses of 500-1000 mg IM have been used for pain of colic and postsurgery (122D).

2. Morphine--Horses become excited at doses above 200 mg IV; below 200 mg, sedation is not outstanding. To avoid excitement, morphine should be combined with a tranquilizer (122D).

3. Pentazocine (Talwin) 200-400 mg IV (122).

Tranquilizers--

1. Chlorpromazine hydrochloride is contraindicated in horses. It produces severe hypotension and excitement (122D).

2. Promazine hydrochloride 0.5-1 mg/kg IV or IM (122D).

3. Acepromazine 0.05-0.1 mg/kg. Large doses produce excitement (122D).

4. Xylazine (Rompun) is currently considered the best sedative in horses. Within 15-20 minutes, it produces deep sedation that lasts for 30 minutes (122D). Xylazine by the IV routes has sedated horses to the point where they were almost unable to support themselves; 1.1 mg/kg IV or 2.2 mg/kg IM provided good sedation. Atropine sulfate 0.011 mg/kg IV was administered to prevent second-degree atrioventricular block induced by IV xylazine. Following administration of xylazine, horses were satisfactorily anesthetized with thiamylal sodium and halothane (56).

Muscle Relaxants (122D)--Muscle relaxants are used to facilitate endotracheal intubation, control movements and kicking during inhalation anesthesia induction, and provide relaxation as indicated for surgery. Muscle relaxants should not be used without adequate equipment for artificial ventilation nor used without analgesics.

1. D-tubocurarine. Doses which prevent motor response to stimulation also impair respiration. A dose of 0.2 mg/kg produces respiratory paralysis.

2. Gallamine triethiodide 0.11 to 0.22 mg/kg produces complete muscle relaxation and respiratory arrest for 10-20 minutes, which can be reversed with 30-60 mg atropine plus 10 mg neostigmine. Its use in the horse is not recommended.

3. Succinylcholine chloride 0.12 to 0.15 mg/kg IV will produce paralysis without serious respiratory embarrassment. Doses of 0.1 mg/kg may be administered as required during surgery. Dilute solutions may

be infused at a rate of 0.03 mg/kg per minute. It is rapidly hydrolyzed, therefore short-acting (2-3 min). IV administration produces tachycardia, increased blood pressure, and arrhythmias. Doses of 0.18 mg/kg IV have been used to cast horses; however, its use for this purpose is questionable since bradycardia, cardiac irregularities, and cardiac arrest may occur. A large percentage of horses develop endocardial hemorrhage.

4. Guaiacol glycerine ether produces depression and drowsiness. To cast a horse, 0.08-0.1 g/kg IV is administered in a 5% solution. A 500-kg horse would receive 1 liter of a 5% solution. Action lasts 10-15 minutes, and there is a wide margin of safety. Thiopental sodium may be combined at a dose of 5 mg/kg.

A general anesthesia should be used with muscle relaxants. The effectiveness of local anesthetics is difficult to assess in a paralyzed animal.

Basal Narcosis--Basal narcosis is depression without analgesia. Chloral hydrate 4.0-4.5 g/50 kg IV is administered as a 10% solution. Chloral hydrate is irritating and should not be administered outside the vein. Horses recover sufficiently to be able to stand within 1 hour. To prolong narcosis, pentobarbital sodium IV should be administered slowly to effect. Basal narcosis is often supplemented with regional anesthesia (122D).

Inhalation Anesthesia

Inhalation anesthetics are administered to horses by the semiopen or closed (or semiclosed) technics. Chloroform is the only agent that can be satisfactorily administered through a face mask containing a sponge soaked with the anesthetic. Anesthetic circuits (circle and to-and-fro) have been devised for large animals. Because of its potency and low toxicity, halothane is the inhalation anesthesia of choice in the horse (122D).

Technics for preoperative preparation and intubation of the horse have been described and illustrated by a series of photographs (83).

Preanesthetic medication is used to decrease excitement in the horse prior to anesthesia (112). Agents frequently used are tranquilizers acetylpromazine 0.04 mg/lb (0.09 mg/kg) IV, promazine 0.5 mg/lb (1.1 mg/kg) IV, and xylazine 0.25-0.5 mg/lb (0.55-1.1 mg/kg) IV; the narcotic meperidine 0.5 mg/lb (1.1 mg/kg); and atropine 0.02 mg/lb (0.04 mg/kg) subQ or IM. Induction technics include inhalation anesthesia via a mask or rapid IV injection of sodium thiamylal or sodium thiopental 3 g/1000 lb (450 kg) if tranquilized or 4 g/1000 lb (450 kg) if not tranquilized. Animals must be protected from injury when they fall. Gradual induction may be achieved by administering a muscle relaxant, 1000 ml 5% glyceryl guaiacolate, plus 2 g thiamylal or thiopental IV for a 1000-lb (450-kg) horse. Following induction the horse is intubated and maintained on halothane or methoxyflurane. The initial concentration of halothane administered is 5%, which is reduced to 0.5%-1% for maintenance. Methoxyflurane is initially administered at a 3% concentration and reduced to 1% for maintenance. The most

dangerous time is often during recovery when animals sometimes become fractious; they can injure themselves and their handlers (112).

Halothane anesthesia produces respiratory depression characterized by a decrease in rate and tidal volume. Alveolar collapse and right-to-left shunts result in hypercapnia and respiratory acidosis. Assisted respiration has prevented alveolar collapse and maintained normal pH and carbon dioxide tension. Horses with assisted respiration had higher O_2 tension values and were able to regain their feet in less time after anesthesia than horses whose respiration was unassisted. Premedication with a tranquilizer (12.8 mg/kg IV propiopromazine) and atropine sulfate 2 mg/100 kg plus thiopental sodium 0.8 g/100 kg IV for anesthetic induction produced only slight changes in P_{CO_2} and pH (116).

Large animal anesthesia equipment is available from several manufacturers; the references for equine anesthesia (83, 112, 113, 116, 122D) should be consulted for detailed description of such equipment.

Intravenous Anesthesia

Thiopental sodium 1 g/90 kg may be administered by rapid IV injection. Within 30-40 seconds the horse is unconscious and relaxed, and surgical anesthesia is sufficient to perform short surgical procedures and castration. To prevent violent recoveries, a tranquilizer should be administered as a preanesthetic. Hobbles should be applied to prevent the horse from rising as anesthesia lightens. Following administration of thiopental sodium, a light dose of succinylcholine 0.1 mg/kg IV may be administered to facilitate endotracheal intubation. Pentobarbital 1 g IV plus the recommended dose of promazine or acetyl promazine is used for sedation without casting (122D).

ANESTHETIZING NONHUMAN PRIMATES

Preanesthetics

Anticholinergics--Atropine sulfate 0.04 mg/kg IM.

Narcotics--

1. Morphine 1-3 mg/kg subQ produces mild depression and analgesia in the chimpanzee. Most primates require the same dose range as the dog, 0.5-0.75 mg/kg, or slightly higher to achieve sedation (122).

2. Meperidine is an excellent preanesthetic for the chimpanzee at a dose of 10 mg/kg IM. The analgesic dosage is 3-5 mg/kg IM (15).

Tranquilizers--Tranquilizers are used as preanesthetics but should not be used alone in large primates, such as chimpanzees, which may present a false appearance of sedation. The following tranquilizers have been used with good results in the chimpanzee (15, 46):

1. Chlorpromazine (Thorazine) 3-6 mg/kg IM.

2. Promazine (Sparine) 100-300 mg IM.

3. Propiopromazine 0.75 mg/kg IM.

4. Oxazepam (Serax) 10 mg per os.

5. Prochlorperazine (Compazine) 10-20 mg IM.

Neuromuscular Blockers--

1. Succinylcholine 2 mg/kg IV has been used for chemical restraint and in conjunction with local or general anesthetics (68).

2. D-tubocurarine. The paralyzing dose is 0.09 mg/kg (69).

Inhalation Anesthesia

A number of technics may be used for anesthetic induction prior to maintenance with an inhalation anesthetic:

1. The short-acting barbiturates such as thiamylal 2.5% or thiopental sodium 2.5% IV may be administered through a catheter placed in the cephalic or popliteal vein, followed by intubation (79).

2. Halothane (3% concentration) has been administered through a human pediatric face mask. For small primates such as prosimians, the open endotracheal tube can be used to cover the nostrils. Inhalation induction is ideal for small primates whose veins may be difficult to catheterize (79).

3. Baboons anesthetized for neurosurgery have been induced with phencyclidine HCl 1 mg/kg IM plus 2.5% thiopental sodium IV to effect. The larynx was sprayed with cetacaine and an endotracheal tube was passed. N_2O (60%) and O_2 (40%) were administered at 3 liters/min for 2-3 minutes, with every third or fourth inspiration assisted. The total flow was decreased to 2 liters/min with 1:1 H_2O-O_2 and 0.25% halothane. The halothane was gradually increased by 0.1% increments up to a maximum of 1% as the phencyclidine was metabolized and excreted by the kidneys (99).

4. Anesthetic chambers have been used to induce primates that are fractious or difficult to restrain (58).

An anesthetic chamber containing 4% halothane in oxygen has been used for anesthetic induction of the squirrel monkey. Following induction the animals were intubated and maintained on 1%-2% halothane (63).

At USAFSAM, induction is with 2.5% thiopental sodium 25 mg/kg IV, titrated to effect. Atropine 0.04 mg/kg subQ is administered. Following intubation, the inhalation anesthetic technic described on page 49 is used. Because of its rapid induction and recovery, halothane is preferred over methoxyflurane (51). For small primates, a pediatric circle system (semiopen) with high flow rates is used to decrease dead space.

At the Holloman colony halothane was the inhalation anesthetic of choice for the chimpanzee. Their technics for administering the halothane have been described in detail (15, 105A).

The cardiovascular effects of halothane have been studied in the stumptailed macaque (Macaca arctoides). During both spontaneous and controlled ventilation, cardiovascular function progressively decreased as anesthesia increased from 1 to 2 MAC (minimum alveolar concentration of anesthetic to prevent gross, purposeful movement in response to a painful stimulus). Mean arterial pressure decreased 40%-50%, and cardiac output decreased 20%-60%. Cardiac dysrhythmias occurred in all monkeys, with no relationship between anesthetic level or ventilation. Cardiovascular depression was less with spontaneous than with controlled ventilation. Positive intrapleural pressure due to controlled ventilation decreased venous return; hypocapnia due to controlled ventilation should also decrease sympathetic stimulation. Hypercapnia and atelectasis are problems of spontaneous ventilation; therefore, it is recommended that controlled ventilation be administered using a low inspired to expired time ratio to decrease the total period of elevated intrathoracic pressure and at a rate to maintain normal P_{CO_2} values. Halothane in M. arctoides had a greater depressant effect upon circulation and a smaller margin of safety than in the dog or man (124).

The addition of N_2O to halothane has resulted in significantly less depression than halothane alone during spontaneous breathing. Similar findings are observed in man (123).

Halothane anesthesia has been used for cesarean sections in primates. The mother was maintained on light surgical anesthesia. Depression of the infant disappeared after the first few breaths (79).

Injection Anesthesia

Dissociative agents--

1. Phencyclidine (Sernylan). Doses ranging from 0.25 to 5 mg/kg IM produce sedation to catalepsis and analgesia. Doses above 5 mg/kg IM produce tonic clonic seizures or involuntary movements resembling an inadequate dosage. Since it provides little or no muscle relaxation, phencyclidine's value as the sole anesthetic agent is questionable (79). Subcutaneous administration prolongs the induction and recovery times and, therefore, is not used. IV administration has the same effects as IM but with a shorter induction period. Table 2 shows the dose-related effects of IM and oral phencyclidine in Macaca mulatta (82). Atropine sulfate 0.04 mg/kg should be administered as a preanesthetic to prevent excess salivation.

Phencyclidine supplemented with short-acting thiamylal or thiopental barbiturates provides good anesthesia. The barbiturates should be titrated to effect since the dose is greatly reduced when combined with phencyclidine (82). Phencyclidine combined with barbiturates may produce respiratory depression (99); therefore, all animals should be intubated and assisted every fourth or fifth inspiration.

TABLE 2. ADMINISTRATION OF PHENCYCLIDINE TO MACACA MULATTA (82)

Av. dose (mg/kg)	Av. time to onset (min)	Effect	Av. time to recovery (hr)
Intramuscular			
0.25	2	Calmness	0.5
0.5	2	Analgesia	1
0.75	3	Catalepsy	1.5
1.0	5	Surgical anesthesia	2
1.5-5.	5	Surgical anesthesia	2-4
5 & over	6	Clonic spasms progressing to intermittent convulsions	4-6
Oral			
0.75	55-65	Calmness to analgesia	2
1.0	55	Analgesia	2
2.0-5.0	45-55	Surgical anesthesia	4

Small doses of phencyclidine can be repeated as needed without adverse effects. Phencyclidine 0.25-0.5 mg/kg IM plus a local anesthetic at the incision site provides adequate restraint to perform a cesarean section without fetal depression (82).

Phencyclidine administered to the baboon at a dose of 1.2 mg/kg IM produced ataxia within 2-3 minutes and a recumbent state lasting 2-19 minutes. Complete recovery required 1-7 hours (133).

Phencyclidine (Sernylan) is frequently used to restrain chimpanzees and possesses a wide margin of safety. Stimulation rather than depression may occur in an occasional animal. Phencyclidine should not be used when electroencephalograms are to be recorded since they are adversely affected by the drug. The chimpanzee should be fasted 12-18 hours and administered atropine sulfate 0.2-0.4 mg as a preanesthetic. For chimpanzees smaller than 23 kg, phencyclidine 0.2 mg/kg IM may be used for tranquilization; larger chimpanzees may be aroused at this dose and be extremely dangerous. Phencyclidine 0.5-0.7 mg/kg IM is adequate for procedures such as blood collection, radiology, and physical examination; a dose of 0.8-1.0 mg/kg IM provides anesthesia for 30-50 minutes, adequate for minor surgery. Anesthesia may be prolonged by administering supplemental doses of phencyclidine 0.5 mg/kg IM at 30-min intervals or with IV pentobarbital sodium or thiopental (15, 46).

Phencyclidine is not recommended for the owl monkey (Aotus trivergatus) because of prolonged recovery times and residual effects which could affect experimental data. A dose of 1 mg/kg IM produced catalepsy to deep sedation, with recovery requiring 3-7.5 hours; 2 mg/kg IM had a recovery period of 8-14 hours, with residual effects lasting up to 24 hours; 3 mg/kg IM had a recovery period of 8.5-14 hours, with residual effects up to 36 hours (9).

2. Ketamine. Ketamine is routinely used in nonhuman primates. Data from 615 nonhuman primates anesthetized a total of 1,039 times with ketamine have been reported. Very young animals required higher dosages per kilogram than did middle-aged adults; likewise, smaller species required a higher dosage than the larger species. Induction was rapid, less than 6 minutes. Duration of anesthesia was 20-55 minutes, with complete recovery in 1-3 hours. Atropine (0.04 mg/kg) should be administered to control salivation. Rapid administration or high dosages of ketamine produces some respiratory depression; therefore, agents which depress respiration should be used cautiously when administered in conjunction with ketamine (7). Table 3 lists suggested initial dosages of ketamine by species for chemical restraint and surgical anesthesia.

TABLE 3. SUGGESTED INITIAL DOSAGES OF KETAMINE FOR PRIMATE SPECIES (7)

Species	Chemical Restraint (mg/kg)	Surgical Anesthesia (mg/kg)
A. trivirgatus	10.0-12.0	20.0-25.0
C. capuchin	13.0-15.0	25.0-30.0
C. torquatus atys	5.0- 7.5	10.0-15.0
C. aethiops	10.0-12.0	25.0-30.0
E. patas	3.0- 5.0	5.0- 7.5
G. gorilla gorilla	7.0-10.0	12.0-15.0
H. lar	5.0-10.0	10.0-12.0
L. catta	7.5-10.0	10.0-12.0
M. fascicularis-irus	12.0-15.0	20.0-25.0
M. fuscata	5.0	
M. mulatta	5.0-10.0	20.0-25.0
M. nemestrina	5.0- 7.5	20.0-25.0
M. radiata	12.0-15.0	25.0-30.0
M. silenus	10.0-12.0	
M. speciosa	5.0- 7.5	20.0-25.0
M. talapoin	5.0- 7.5	10.0-12.5
P. troglodytes	5.0- 7.5	10.0-15.0
P. anubis	5.0- 7.5	10.0-15.0
P. cynocephalus	5.0- 7.5	7.5-10.0
P. papio	10.0-12.0	
P. pygmaeus	5.0- 7.5	12.0-15.0
P. entellus	2.0- 3.0	3.0- 5.0
S. sciureus	12.0-15.0	25.0-30.0
S. syndactylus	5.0- 7.0	7.0-10.0

Infant Macaca nemestrina 19-35 days old and weighing 450-865 g were successfully anesthetized for a 3-4-hour surgical procedure, using ketamine 18 mg/kg IM and sodium thiamylal 15 mg/kg IV. Ketamine and sodium thiamylal are short-acting anesthetics in adult monkeys; however, in the infant they are relatively long-acting--9.4 hours when thiamylal was used alone and 4.8 hours when combined with ketamine. Successful

anesthesia in infant monkeys required monitoring and controlling body temperature, respiration, and pulse during surgery and adequate hydration and body temperature maintenance postoperatively (12).

Twenty-five chimpanzees were anesthetized a total of 975 times during a 28-month period. To produce restraint, a mean dose of 9.2 mg/kg IM ketamine was administered. Induction time was 4.9 minutes; anesthetic time, 26.1 minutes; and recovery time, 57.6 minutes. Tolerance to repeated injections was not evidenced by shortened anesthetic time (61).

3. CI-744 is a combination of tiletamine (CI-634), a dissociative agent, and flupyrazapon (CI-716), a tranquilizer. This combination provided excellent surgical anesthesia with good muscle relaxation. The dose for primates was 2-6 mg/kg IM; induction time, 30 seconds to 6 minutes. The anesthetic time increased as the dose of CI-744 was increased, and varied with individual species. Full recovery occurred 1 hour after righting reflexes were regained. Pharyngeal and palpebral reflexes were maintained in all animals. CI-744 is a safe agent with a wide range of doses and easy to administer (14, 90).

Innovar-Vet--The combination of droperidol (a tranquilizer) and fentanyl (an analgesic narcotic) produces profound tranquilization with a reduced pain response. It may be administered either IM or IV and is used for minor surgical procedures. Atropine is administered to prevent bradycardia. The fentanyl portion may be reversed with nalorphine HCl. The IM dose is 1 ml/9 kg for most primates. For the squirrel monkey (Saimiri) the dose is reduced to 0.05 ml/kg IM (15, 122B).

Innovar-Vet and phencyclidine combinations have been used. The animal was first sedated with phencyclidine 1-3 mg/kg IM, followed with Innovar-Vet 1 ml/18 kg. This combination produced stage III, plane 1 or 2, surgical anesthesia; muscle relaxation was fair. The period of effectiveness is limited by the fentanyl portion of the Innovar-Vet. The phencyclidine may produce shallow respiration, and ventilation may need to be assisted to insure adequate gas exchange (79).

Innovar-Vet 0.05 ml/kg IM has been used in chimpanzees with unpredictable results (15).

Barbiturates--Only the short-acting barbiturates, thiamylal or thiopental, are recommended. They are used primarily for induction to enable intubation prior to administering an inhalation anesthetic or for short procedures lasting 10-15 minutes. We use 2.5% thiopental sodium 1 ml/kg IV administered through an intercath placed in the popliteal vein. The intermediate barbiturates such as pentobarbital (30 mg/kg IV) are unsatisfactory because of their long recovery periods of 4-5 hours or more.

The chimpanzee does not appear to go into an excitatory stage when barbiturates are administered. Thiopental sodium or pentobarbital sodium are administered at a dose of 30-35 mg/kg IV (15).

ANESTHETIZING RATS

Inhalation Anesthesia

Volatile anesthetics (ether, methoxyflurane, and halothane) have been administered by means of anesthetic chambers, nose cones, masks, and tracheostomy (69).

Inhalation anesthesia, with an anesthetic machine and a pediatric mask that could be placed over both the nose and mouth for minimal leakage, consisted of an initial mixture of 40% ether, 50% N_2O, and 10% O_2. To prevent breath-holding, a small amount of carbon dioxide was added to stimulate regular breathing. During surgery, a 50% ether, 35% N_2O, and 15% O_2 mixture was used. To terminate anesthesia, a 70% O_2, 20% helium, and 10% CO_2 mixture was administered for 5 minutes, followed by 100% O_2. The rats awakened in about 7 minutes. This technic was used for 250 rats (45).

A multicompartment, plastic, anesthetic box utilizing methoxyflurane was used to anesthetize up to 10 rats at one time for interim and terminal bleeding prior to necropsy for toxicologic studies. The degree and duration of anesthesia could be controlled for each compartment (89).

A technic has been developed and described for intubating rats so that halothane anesthesia may be maintained with a closed-circuit anesthetic machine (137). The rats were wrapped with a towel and induced with halothane by means of either a nose cone containing halothane or a syringe barrel attached to a halothane-oxygen-primed anesthetic machine. The tracheal cannula assembly consisted of a 14-ga 4-in (10-cm) stainless steel cannula with stylet and spatula (52).

The rat has been resuscitated by modified mouth-to-mouth ventilation: holding rubber tubing over the nostrils and mouth, the operator breathes rapidly in the other end. Care is taken to not overinflate the lungs (87A).

Injection Anesthesia

Intravenous anesthesia is administered through the saphenous or the tail vein. To aid in visualizing this vein, the cornified skin layers may be scraped off, heat may be applied to the tail by a heat lamp or immersion in hot water, or a venous cutdown may be performed. Intracardiac and intramedullary routes are rarely used (87A).

Chloral hydrate, chlorbutanol, chloralose, urethane, and paraldehyde possess many disadvantages and are rarely used (69).

Pentobarbital sodium 30-40 mg/kg IV or IP produces anesthesia in 5-15 minutes and lasts for 45 minutes. To prolong anesthesia, 25% of the original dose may be administered as required. The LD_{50} varies between 48 and 100 mg/kg because of age, sex, weight, and strain differences (122A). Progressively increasing doses of pentobarbital sodium (20 mg/kg per step) were administered by the IP route at 7-day intervals

in 7 strains of adult male mice. The LD_{50} was achieved at a significantly lower dose for 4 albino strains (60-70 mg/kg) than for 3 pigmented strains (90-120 mg/kg). The total sleeping time was also decreased in the pigmented strains (106).

Rats (Rattus norvegicus) have been anesthetized with ketamine HCl 44 mg/kg IM. Anesthesia was satisfactory for heart puncture, laparotomy, and skin grafting. Recovery occurred within 15-25 minutes. Excess salivation was controlled by administering atropine 0.04 mg/kg IM (138).

CI-744 20-30 mg/kg IP has produced satisfactory anesthesia. Sleeping time averaged 68-90 minutes; induction time, 3 minutes. Relaxation was excellent (134).

Rats averaging 298 g were sedated with 0.13 ml/kg IM Innovar-Vet. Induction time averaged 5-8 minutes; anesthesia, 30 minutes. The rats were alert and appeared to return to normal activity in 1-2 hours (66).

ANESTHETIZING MICE

Survival is increased when appropriate postanesthetic care is provided. Temperature should be maintained at 80°-85°F (27°-30°C). Fluids, 0.5 ml 20% glucose or 0.25 ml 0.85% NaCl, may be administered IP.

Inhalation Anesthesia

Technics similar to those described using ether, methoxyflurane, and halothane for rats and guinea pigs have been administered through chambers, nose cones, and masks.

Ether induction in a closed chamber, with maintenance by a small nose cone, resulted in profuse salivation and mortality as high as 50% during major surgery (122A). Chloroform is contraindicated in male mice of the C3H, DBA, CBA, C_6H_f, A, Balb-C, and HR strains. Marked liver and kidney damage results in high mortality (87L, 118, 122A).

Many mice were anesthetized in a closed-system chamber for up to 60 minutes. For CO_2 absorption, a bed of soda lime covered the bottom of the chamber. Fluothane or methoxyflurane was used alone or in combination with nitrous oxide. Halothane administered through a Fluotec vaporizer was considered the most effective anesthetic (11).

The effect of methoxyflurane on C3H/HeJ male mice 3.5 months old and weighing 30 g each was studied. A beaker containing methoxyflurane was placed in a closed chamber. Exposures of 20 minutes or less produced no mortality in normal mice; above 20 minutes, the incidence of mortality increased. Mice in the chamber for 10-20 minutes remained anesthetized for 5-10 minutes when exposed to room air. When respirations decrease below 10/10 sec, the mice should be removed from the chamber. A complicating factor is anoxia and carbon dioxide accumulation in such closed chambers (44).

A technic for endotracheal intubation and the administration of positive-pressure oxygen in mice undergoing surgical removal of the thymus gland has been described (114). The apparatus consisted of three parts: (1) flow valve, bubble meter, high-pressure-limit assembly; (2) positive-pressure valve; and (3) endotracheal catheter, Teflon "spaghetti" tubing 0.222-0.344-in (0.56-0.87 cm) diameter.

Injection Anesthesia

Intravenous anesthesia is administered with a 1-ml tuberculin syringe and a 25-27-ga needle through the lateral tail vein. Warming the tail with a 100-W bulb or by hot-water immersion produces vasodilation to facilitate venipuncture (122A).

Pentobarbital sodium 40-70 mg/kg IV or IP had an induction time of 5-10 minutes and a duration of 20-30 minutes; mortality was below 10% (87L). At a dose of 80-90 mg/kg IV or IP, mice have exhibited a wide variation in response--from death to not being anesthetized (122A). In mice anesthetized with pentobarbital, males appear to sleep longer than females (87L, 122A). The lower dosage range of pentobarbital can be used if a preanesthetic such as chlorpromazine 50-60 mg/kg IM is administered or the pentobarbital anesthesia is supplemented with inhalation anesthesia (122A). Thiopental 25-50 mg/kg IV and hexobarbital 100 mg/kg IP have been used in the mouse (87L).

Mice have been satisfactorily anesthetized with ketamine 44 mg/kg IM and atropine 0.04 mg/kg. Orbital sinus puncture, venous cutdown, and laparotomy procedures were performed. Recovery occurred within 15-30 minutes (138).

A 10% solution of Innovar-Vet in physiological saline was used to anesthetize mice averaging 27 g in weight. A dose of 0.002 ml/g IM 10% Innovar-Vet provided satisfactory anesthesia to perform trunk skin grafts and orbital bleeding; 0.005 ml/g IM provided deep anesthesia for performing splenectomies (66).

ANESTHETIZING GUINEA PIGS

Inhalation Anesthesia

Methoxyflurane is considered the inhalation agent of choice (25, 69, 105B). Anesthetic deaths are 2% with methoxyflurane, 8% with ether, and 13% with pentobarbital (87E). Induction may be in an anesthetic chamber or Bell jar. Maintenance anesthesia can be supplied using a nose cone constructed of blotter paper and filled with gauze, with the anesthetic dripped on the cone. To maintain a smooth anesthetic plane, the distance between the nose and cone may be varied. A modified mouth-to-mouth resuscitation technic has been described using a 1-in-diameter (2.5-cm-dia) hollow tube placed over the mouth and nostrils. The fingers are pressed under the sternum against the diaphragm to determine if the lungs are being over distended (87E).

Ether has been administered in an ether jar or face mask. To prevent copious secretions, 0.25 mg atropine was required (122A). When 0.4 mg atropine was administered with ether anesthesia, excess bleeding occurred during surgery (87E). This high dose of atropine probably accelerated heart rate and blood pressure, which caused the increased bleeding.

Injection Anesthesia

Intravenous anesthetics are difficult to administer because of the small size of the peripheral vessels. A 26-28-ga needle may be used for the lingual vein, marginal ear vein, or the dorsal vein of the penis. Intraperitoneal injections are dangerous because of the large size of the urinary bladder, the gallbladder, and the liver (87E, 122A).

Pentobarbital sodium 28 mg/kg IP had an induction period of 15 minutes and produced anesthesia that lasted 1-2 hours. Complete recovery has taken as long as 12 hours (25). Pentobarbital has been used with a number of preanesthetics. Chlorpromazine 25 mg/kg IM plus 30 mg/kg IP pentobarbital had an induction period of 15 minutes and produced surgical anesthesia lasting 50 minutes (122A). Pentobarbital 10 mg/kg IM has been combined with procaine HCl 300 mg/kg IM; and pentobarbital 30 mg/kg IM with meperidine 2 mg/kg (87E). The LD_{50} was reached at a lower concentration of pentobarbital when administered with procaine or meperidine. Pentobarbital sodium is contraindicated for cesarean sections in the guinea pig because of neurological sequelae in the newborn (122A).

Adult guinea pigs averaging 926 g assumed a relaxed limp posture when given Innovar-Vet 0.08 ml/kg IM. Anesthesia was sufficient to perform cardiac punctures. Sedation lasted approximately 30 minutes and could be prolonged by injecting 25%-50% of the initial dose (66). Innovar-Vet 0.44 ml/kg IM provided anesthesia adequate for laparotomy but inadequate for eye enucleation; 0.88 ml/kg IM was most desirable for both procedures. The guinea pigs were unable to right themselves for 120 minutes. Foot retraction, corneal, and auditory reflexes were absent 180, 150, and 150 minutes respectively. For surgical anesthesia, 0.66-0.88 ml/kg IM is recommended as a safe dose (103).

Ketamine HCl 22 mg/kg IM provided sedation sufficient to decrease pain reception for 5-10 minutes to enable venous cutdowns. Dorsal recumbency was resisted. Recovery was rapid, with excess salivation in 50%. Ketamine 44 mg/kg IM plus atropine 0.4 mg/kg IM abolished pain perception for 15-25 minutes to permit general surgery (laparotomy). Dorsal recumbency was not resisted, and recovery was rapid (138).

CI-744 was not considered a satisfactory anesthetic in guinea pigs at doses up to 80 mg/kg IM, since they failed to become adequately relaxed and responded to external stimuli (134).

Epidural anesthesia has been used to perform adrenalectomies. Chlorpromazine 2 mg/100 g was administered in the axillary fold. A 23-ga 1-in (2.5-cm) needle was inserted into the lumbosacral space, and warm 1% lidocaine 0.2-0.25 ml was injected slowly. The effect was prompt and lasted 40-50 minutes (69).

Epidural anesthesia has also been administered through an intravenous catheter. The catheter was passed through a 19-ga needle inserted into the intervertebral space at the lumbosacral level. The catheter was advanced 1 cm into the canal and secured by a suture in the skin after the needle was removed. Warmed to body temperature, 1% lidocaine with 1:100,000 epinephrine was injected at a rate of 0.2 ml for guinea pigs weighing less than 500 g and 0.25 ml for those larger than 500 g. Onset was prompt and anesthesia lasted 40-50 minutes. Anesthesia could be prolonged by repeated injections through the catheter, titrated to effect. A preanesthetic tranquilizer (propriopromazine) was administered by the subcutaneous route at a dose of 5 mg/300 g or smaller, 7.5 mg/300-500 g, and 10 mg/500 g or larger guinea pigs 15-30 minutes before lumbosacral catheterization (128). Recovery was complete in 2-3 hours.

ANESTHETIZING RABBITS

The rabbit is very difficult to anesthetize, and susceptibility to anesthesia varies widely. For surgical anesthesia, the rabbit has a large dose range for many anesthetics. The margin of safety between surgical anesthesia and death is narrow for barbiturates, ether, chloral hydrate, and paraldehyde (71). The inhalation anesthetics are safer and easier to control; however, the rabbit is difficult to intubate because of a relatively long curved mouth and a narrow opening that makes it hard to visualize the larynx. The standard eye-blink reflex is not reliable in the rabbit since it often persists after the surgical stage of anesthesia has been achieved. Depth of anesthesia is usually monitored by respiration and the toe-pinch reflex. Respiration should remain regular, deep, and slow; when it becomes shallow and intermittent, anesthesia is too deep (87I). The normal respiratory rate is 60/min; surgical anesthesia is achieved when the rate is 15-20 min. Respiration should not be allowed to decrease below 15/min. The rabbit is unique in that its liver contains large quantities of atropine esterase; therefore, it can tolerate large doses of atropine (87I).

Preanesthetics (69)

Atropine sulfate 0.04 mg/kg IM.

Acetylpromazine 1 mg/kg IM.

Chlorpromazine 7.5 mg/kg IV; 25-100 mg/kg IM produced severe necrotic lesions in the thigh muscle.

Diazepam 5-10 mg/kg IM.

Propiopromazine 5-10 mg/kg IM.

Inhalation Anesthesia

Inhalation anesthesia is the route of choice in the rabbit. Induction has been with short-acting barbiturates or with inhalation anesthetics administered by face mask, anesthetic chambers, or endotracheal tube.

Intubation--A variety of technics have been developed to intubate the rabbit, a difficult species to intubate (50). Rabbits have been intubated while awake without the use of preanesthetics. The animal was placed in a restraint box and a 4-in (10-cm) 17 French cuffless endotracheal tube of semirigid plastic tubing was used. The rabbit was given pure oxygen to breathe until respiration was normal, then anesthesia was induced with methoxyflurane (50).

Ketamine HCl diluted 1:2 with 0.85% saline has been injected in the marginal ear vein at a dose of 15-20 mg/kg and a rate of 100 mg in 10-15 seconds. This subanesthetic dose of ketamine permitted smooth endotracheal intubation and induction. A Miller #2 laryngoscope blade was modified by wrapping it with 0.5-in (1.3-cm) adhesive tape to prevent the rabbit's upper incisors from obstructing the view. A 3-mm-ID endotracheal tube was used (67).

Rabbits premedicated with 10 mg/kg acetylpromazine maleate and 0.3 ml/kg paraldehyde became quiet in 15-30 minutes. When quiet, the rabbit was placed in a cat bag, with its head exposed. The neck was hyperextended, and a wood-dowel mouth gag with a hole in it was placed in the mouth. A tapered 16 French endotracheal tube, 2.5-mm ID, was passed through the hole in the mouth gag. As the tube reached the epiglottis, the larynx was compressed with the fingers so the rabbit would gasp and the tube could be inserted into the trachea. Cetacaine spray applied to the larynx was considered undesirable because it decreased the gasp reflex, making intubation more difficult. Edema of the glottis during intubation caused death in 4% (34).

Rabbits have been intubated after 4%-5% halothane was administered through a modified Ayres T-piece and a nose cone. When its jaw was completely relaxed, the rabbit was intubated with a clear, soft 3.5-mm Portex endotracheal tube, 12 cm long, with a wire stylette. A Miller 0 neonatal laryngoscope blade (4.5 cm long) with a penlight handle was used to view the larynx. To permit an adequate view, the laryngoscope blade was placed completely to the left of the upper incisors and parallel to the floor of the mouth. The tongue had to be maintained in the midline (26).

Face Mask--Rabbits have been premedicated with acetylpromazine maleate 1 mg/kg given 1-1.5 hours before inhalation anesthesia to minimize motor activity during induction with methoxyflurane. When methoxyflurane was used without a preanesthetic, several animals went through a period of violent motor activity lasting 5-10 minutes, which resulted in compression fractures of the lumbar vertebrae. Methoxyflurane anesthesia was induced by using a nose cone, and care was taken to prevent the fur around the nose from being soaked in the anesthetic (71).

Rabbits have been induced with acetylpromazine maleate 1 mg/kg, followed by methoxyflurane administered by the open-drop technic, using a 500-ml plastic bottle modified as a mask. Anesthesia was maintained with 0.5% methoxyflurane administered in a 1:2 O_2-N_2O gas mixture at a flow rate of 3 liters/min through an open nonrebreathing system using a face mask. No deaths occurred during 200 procedures (57).

An anesthetic chamber has been used for halothane induction and a face mask for maintenance. Mortality was less than 1% (117).

Promazine 25 mg/3.6 kg or 50 mg/4.1-5.4 kg IM, plus ketamine 200 mg/3.6-5.4 kg IM, have been used as a preanesthetic to provide sedation and analgesia. Twenty minutes later 0.5-1.5% halothane in a 1:1 O_2-N_2O gas mixture was administered via a face mask (19).

Injection Anesthesia

Intravenous Anesthesia--The marginal ear vein or cephalic vein is used for administering intravenous anesthetics. Barbiturates are considered dangerous for the rabbit (71, 137, 138).

Barbiturates possess a wide dose range to achieve surgical anesthesia because of a great variation in individual response. There is usually a narrow margin of safety between surgical anesthesia and respiratory arrest(40). Thiamylal sodium is the most adaptable anesthetic. The 1% concentration provides the most control and least respiratory arrest. The dose range is wide, between 22.85 and 54 mg/kg, and induction is within 3 minutes. Adequate surgical anesthesia lasts only 10 minutes, and recovery occurs within 5-15 minutes. There is no advantage in using the preanesthetics meperidine or morphine with atropine before administering the thiamylal. Pentobarbitone sodium provides a narrow margin of safety.

Pentobarbitone 30 mg/kg IV has provided a wide variation in dose response and a narrow margin of safety, with arousal time varying from 1-10 hours. In one study 30 mg/kg IV pentobarbital resulted in 12 deaths in 68 rabbits anesthetized (69).

The main cause of death with the barbiturates is respiratory depression. Respiratory stimulants are not very effective in treating this depression. Positive-pressure resuscitation using an endotracheal tube is the best supportive therapy. When used as a preanesthetic for the barbiturates, tranquilizers decreased the anesthetic dose, decreased apprehension, and prolonged the anesthesia (87I).

Ketamine HCl 22 mg/kg IV is considered unsafe. A dose of 11 mg/kg IV was safe; however, induction time was almost zero and recovery time was so accelerated that surgical anesthesia lasted only 2-3 minutes (138).

Equithesin IV in the marginal ear vein to effect, following premedication with propiopromazine HCl and paraldehyde, produced unsatisfactory results in 10%-20% of cases studied (69).

Intramuscular Anesthesia--Innovar-Vet 0.17 ml/kg IM provided adequate sedation for procedures such as cardiac punctures and venipunctures. Sedation lasted 30 minutes and could be prolonged by repeated injections of 25%-50% of the initial dose (66).

Ketamine HCl at 22 mg/kg provided adequate sedation for restraint, and at 44 mg/kg for surgical anesthesia. Induction time was 8-10 minutes, and recovery was within 15-20 minutes. Anesthesia could be prolonged with 11 mg/kg IM ketamine administered at 10-min intervals. Preanesthetic atropine SO_4 0.04 mg/kg IM was administered. To provide

muscle relaxation for procedures such as orthopedic surgery, a preanesthetic tranquilizer, triflupromazine HCl 5 mg/kg IM, was administered 30 minutes before administering ketamine HCl at 25%-50% of the normal dose (138).

Ketamine 44 mg/kg IM produced effective analgesia and relaxation in rabbits weighing less than 2.3 kg, and 55 mg/kg IM for rabbits heavier than 2.3 kg. Deep surgical anesthesia was obtained and prolonged by administering methoxyflurane within 5 minutes of the ketamine administration. A nose cone containing cotton was moistened with 2.5 ml methoxyflurane. The nose cone was removed when the respiratory rate decreased below 40 min (136).

The dissociative agents phencyclidine HCl and tiletamine produced catalepsy without suitable analgesia for surgery (21). CI-744, the combination of tiletamine and a tranquilizer (CI-716), was not considered a satisfactory anesthetic in rabbits because they failed to become adequately relaxed and continued to respond to external stimuli. Doses of 12-40 mg/kg IM produced immobilization and dulled reflexes for 40-120 minutes (134). Tiletamine (CI-634) 20 mg/kg IM, followed in 2-3 minutes with chloral hydrate 250 mg/kg IV, was considered both safe and effective for general anesthesia. Surgical anesthesia lasting 1-1.5 hours was satisfactory for abdominal surgery (21).

ANESTHETIZING BIRDS

Many agents are satisfactory for avian anesthesia. Ether, ethyl chloride, halothane, and methoxyflurane are used successfully for inhalation anesthesia. Pentobarbital sodium, chloral hydrate, and tribromoethanol have been administered orally. The parenteral administration of chloral hydrate, pentobarbital sodium, and sodium amytal produced good results when used properly (87D).

A fasting period of 2-3 hours is recommended for birds. Prolonged fasting depletes the liver glycogen reserve, reducing its detoxifying powers. Following anesthesia, birds should be kept in warm quarters 85°-95°F (29°-35°C), turned from side to side at 30-min intervals, and administered oxygen (36, 87D).

Inhalation Anesthesia

Volatile anesthetics must be administered carefully since dangerous concentrations may accumulate in the air-sac system. The anesthetics should be administered intermittently with brief periods of access to fresh air (38).

Ether and ethyl chloride are being replaced by methoxyflurane. For induction, small birds are placed in a glass beaker to which 0.1 ml methoxyflurane has been added. Induction occurs within 30-45 seconds, and anesthesia persists for 2-4 minutes. Maintenance is obtained by using a nose cone fashioned from a disposable syringe container into which cotton is inserted (39, 87D).

Halothane and methoxyflurane have been satisfactorily administered directly into the interclavicular air sac by means of a percutaneously placed polyethylene catheter. This technic has been used for chickens, ducks, sparrows, and turkeys (140).

Induction and maintenance have been obtained by spraying ether and ethyl chloride directly into one nostril. A 2-ml syringe with a 0.25-in (6.25-mm) 26-ga needle is used for ether. Small birds require 0.25-0.5 ml for induction and 0.1-0.25 ml administered intermittently for maintenance (36).

Anesthetic machines may be attached to a large plastic bag placed over the entire bird cage for induction with methoxyflurane. A high oxygen flow of 1 liter/min is used with the vaporizer opened fully. A surgical plane of anesthesia is achieved within 5 minutes. Maintenance is achieved by attaching a small plastic bag ("baggie") to the anesthetic machine, gluing a human baby-bottle nipple to the bag, and cutting a hole in the nipple to enable it to fit over the bird's head (75, 76).

Maintenance anesthesia may be administered through an endotracheal tube in large birds. A series of eagles were induced using a face mask, with a mixture of oxygen and nitrous oxide to which halothane was slowly added; they were then intubated for maintenance (142).

Injection Anesthesia

Intramuscular Anesthesia--Equithesin (chloral hydrate, pentobarbital Na, and magnesium sulfate in an aqueous solution of propylene glycol with 9.5% alcohol) is highly rated for its overall safety and efficiency in birds (38, 87D). Equithesin is injected deep into the breast (pectoral) muscle with a 22-25-ga needle. The dosage recommended is 2.0 ml/kg for weak, debilitated, poor-risk birds and 2.5 ml/kg for healthy birds of all species. Anesthetic induction requires 10-35 minutes, with anesthesia lasting 25-30 minutes.

Pentobarbital sodium (7 mg/ml), at a dose of 1.5 mg for a 35-g bird, injected into the pectoral muscle will induce anesthesia within 2-3 minutes, lasting 30 minutes (30, 31).

Ketamine 25-400 mg/kg produced catalepsy in pigeons. Induction and recovery with ketamine were smooth and uneventful when pentobarbital sodium (20 mg/kg) was used as a preanesthetic. Ketamine 32 mg/kg was injected into the opposite pectoral muscle 10 minutes later and produced anesthesia lasting 40 minutes; 64 mg/kg, 109 minutes. Successive doses of 32 mg/kg ketamine were safely administered at 1-3-hour intervals (13).

Ketamine HCl alone or combined with methoxyflurane is a safe and effective anesthetic for parakeets. Ketamine 1 mg/30 g IM in the pectoral muscle has produced anesthesia within 3 minutes that was adequate for simple procedures such as clipping beaks or taping broken wings. Ketamine 2 mg/30 g IM produced complete anesthesia within 3 minutes, lasting 5-12 minutes; recovery was complete within 20-30 minutes. During recovery, some birds went through an excitatory phase (77). A padded recovery area should be provided (8).

The lethal dose of ketamine in parakeets is approximately 0.5 mg/g body weight. Overdosed birds should receive oxygen and be kept warm and quiet (78).

Ketamine 15-20 mg/kg IM was administered in the pectoral muscle as the sole anesthetic agent in 22 wild birds. To prolong anesthesia, 10 mg/kg could be administered every 5 minutes in healthy birds. Induction occurred within 1-5 minutes; the effects of anesthesia lasted from 30 minutes to 6 hours, depending on the total dose. To enhance the renal excretion of ketamine in debilitated birds, 20-40 ml/kg lactated Ringer's solution was administered subQ (10).

The dosage of ketamine per gram body weight for birds is inversely proportional to the weight of the bird. Baseline figures for ketamine dosage are:

Body weight (g)	mg/g IM
Below 100	0.10-0.2
250-500	0.05-0.1
500-3000	0.02-0.1
Above 3000	0.02-0.05

Immobilizing and lethal doses are also available for a variety of avian species (8).

CI-744 produced adequate anesthesia in the pigeon, but the margin of safety was narrow. A dose of 10-20 mg/kg IM produced immobilization but with poor muscle relaxation; 30-70 mg/kg IM produced satisfactory anesthesia for surgical procedures, averaging 55-90 minutes (134).

Intravenous Anesthesia--Intravenous anesthesia has the advantage of rapid induction and better control of anesthetic stages, and is safer when supplementing the initial dose. The jugular vein is used for small species. For birds the size of a pigeon or larger, the median vein located on the ventromedial surface of the humeroradial joint is used. The bird is restrained on its back with one wing extended and the other folded against the body. Equithesin 1-1.5 mg/kg IV may be administered using a 25-ga needle (87D).

Local Anesthesia

Procaine is considered toxic for birds; however, it has been suggested that this is due to overdosage. Procaine has been successfully administered to pigeons, chickens, and ducks (87D).

ANESTHETIZING AMPHIBIANS AND REPTILES

The anesthetic responses of many reptiles and amphibians vary from those of mammals because of variations in anatomy, physiology, and husbandry. A lowered metabolic rate may prolong the action of an injectable anesthetic and delay recovery for several days. The lack of

a functional diaphragm and the ability of some species to hold their breath and survive for hours by anaerobic metabolism may make it difficult to use inhalation agents for anesthetic induction (16). Anatomy, physiology, and husbandry must be considered when selecting an anesthetic, a technic, and postanesthetic care. Several excellent references (16, 69, 87F) should be consulted.

Frogs and Toads

Hypothermia--Reptiles and amphibians may be restrained or anesthetized by refrigeration for several hours at 5°C or immersion in ice water followed with maintenance in a tray of ice water. Hypothermia may be supplemented with local anesthesia for prolonged surgical procedures. Quick recovery occurs when rewarmed to room temperature (16, 87F).

Inhalation--Frogs are unique in that they breathe through their skin. Ether induction may be accomplished in a Bell jar within 5-10 minutes, or by wrapping the frog with cotton to which the ether is uniformly applied. Anesthesia lasts for several hours (87F).

Methoxyflurane administered to Rana pipiens has a satisfactory margin of safety and a short induction period, and provides deep anesthesia. To insure an adequate and constant vapor pressure, absorbent cotton moistened with 10 ml methoxyflurane is placed in a 1-gallon jar 30 minutes before introducing the frog. A wire-mesh floor is placed over the cotton. A 3/16-in (4.6-mm) hole in the lid will reduce carbon dioxide buildup and oxygen depletion. Deep anesthesia is induced within 2 minutes. The frog is left in the jar for an additional 3 minutes to promote a body anesthetic concentration adequate for surgical procedures. Surgical anesthesia persists for 38 minutes. Recovery is smooth and requires about 7 hours because of the low metabolism of the cold-blooded frog. Pulse and cloacal temperature are unaffected; however, there is a decrease in respiratory rate following induction (135).

Injection--Anesthetic sites are the dorsal lymph sacs, ventral abdominal vein, and ventral lymph sacs. A 25-ga needle is used.

Hexobarbital sodium 120 mg/kg injected into the dorsal lymph sac requires 22 minutes for induction and lasts 3 hours. Pentobarbital sodium 60 mg/kg IV requires 31 minutes for induction and lasts 9 hours. Paraldehyde 4.2 g/kg in the ventral lymph sac produces anesthesia within 15 minutes (87F). Thiobarbital, thiopental, and Dial with urethane are considered toxic and unsuitable for frogs (87F). Ketamine administered either by itself (55-210 mg/kg via dorsal lymph sac) or in combination with methoxyflurane produces severe pulse and respiratory depression and is not recommended for the frog (135).

Immersion--Frogs and toads have been anesthetized by immersing them in tricaine methanesulfonate (MS-222) 0.1% solution, chlorobutanol 0.2% solution for 4-8 minutes, or 10% ethyl alcohol for 10 minutes (69). During anesthesia the frogs should be kept moist and at room temperature, and care taken to prevent drowning. Tricaine methanesulfonate (MS-222),

by immersion or injection, was superior to other anesthetics because of quick induction, rapid recovery, and predictable behavior (139).

Snakes

The depth of anesthesia in snakes may be checked by the tonus of the forked tongue. Surgical anesthesia is achieved when the tongue does not resist being withdrawn with tongue forceps.

Hypothermia--Reptiles and amphibians may be restrained or anesthetized by refrigeration for several hours at 5°C or immersion in ice water followed by maintenance in a tray of ice water. Hypothermia may be supplemented with local anesthesia for prolonged surgical procedures. Quick recovery occurs when rewarmed to room temperature (16, 87F).

Inhalation--Anesthesia in snakes, especially poisonous varieties, can be induced with ether, methoxyflurane, or halothane by soaking a pad and placing it in an enclosed reptile box. Anesthetic chambers using precision vaporizers and CO_2 absorption have been designed for reptiles and small laboratory animals (16). The snake can then be removed and its head placed in a hood containing a pad soaked with the anesthetic. With nonpoisonous snakes and reptiles, anesthesia can be inducted with a mask made from a syringe barrel or plastic bottle neck connected to a nonrebreathing system such as the Ayres T-piece (16). A nonpoisonous snake can also be placed in a clear plastic bag attached to a circle anesthetic machine. Induction with 4% halothane, 72% nitrous oxide, and 24% oxygen requires 20-30 minutes. Following relaxation, the snake can be intubated and maintained on inhalation anesthetics (105D). The glottis, located forward in the mouth and lacking an epiglottis, is not difficult to intubate. Snakes required intermittent positive-pressure breathing with inhalation anesthesia.

Inhalation anesthesia in reptiles requires the following care (16):

1. Prevent respiratory insufficiency by ventilating with 100% oxygen before extubation. If ether or methoxyflurane is used, a longer period of ventilation will be required because these agents are highly soluble in tissues or lipids.

2. Prevent high positive pressure during ventilation because reptiles do not possess a diaphragm and their thoracic cavity is not fixed.

3. The pattern of ventilation should correspond with the normal ventilation pattern for the species; i.e., apneustic plateau or breath-holding for crocodilians.

4. During recovery, the temperature and humidity should be in the normal range for the species.

Injection--Snakes lack heavy muscles; therefore, when the IM route is used, small volumes of anesthesia must be injected at multiple sites (lateral to midline in caudal one-third of body). Intraperitoneal

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injections are made by introducing the needle ventrally into the mid-section of the pleuroperitoneal cavity and avoiding the pericardial cavity (16).

Etorphine HCl 5 mg/kg IM, meperidine HCl 200 mg/kg IM, and oxymorphone HCl 1.5 mg/kg IM appear to have no grossly observable effects in snakes (16).

Tricaine methanesulfonate 15-30 mg/kg IP provides anesthesia lasting up to 60 minutes following an induction period of 12-40 minutes (16, 87F).

Barbiturates such as thiamylal and thiopental administered IP have resulted in high mortality (105D). Thiopental 15-30 mg/kg IP has an induction period of 30-45 minutes and provides anesthesia for 2-6 hours. Pentobarbital sodium 15-30 mg/kg IP has an induction period varying from 5 to 60 minutes and provides deep anesthesia for 15 hours, with complete recovery in 18-36 hours (16).

Turtles and Tortoises

Muscle relaxation is the most reliable guide to the depth of anesthesia. Pupil size is undependable, and corneal reflexes may be present even in deep anesthesia. Respiratory rate is normally very low and variable; therefore, it is difficult to use as a guide.

Hypothermia--Reptiles and amphibians may be restrained or anesthetized by refrigeration for several hours at 5°C or immersion in ice water followed with maintenance in a tray of ice water. Hypothermia may be supplemented with local anesthesia for prolonged surgical procedures. Quick recovery occurs when rewarmed to room temperature (16).

Inhalation--Induction with inhalation anesthetics may be difficult since turtles can hold their breath and convert to anaerobic metabolism. The mouth can be manually opened and the larynx sprayed with a local anesthetic and intubated prior to induction. Following intubation, halothane 3% in oxygen has been used for induction; maintenance anesthesia was with 1.5% halothane (16). Induction in an anesthetic chamber with ether has required as long as 3 hours (43). In 25% of turtles anesthetized with ether, deep anesthesia lasted as long as 10 hours (69, 105D). Methoxyflurane has been used in a chamber to induce anesthesia; maintenance was with a nose cone (69).

Injection--For IV injection, the ventral abdominal vein is approached through a hole drilled in the plastron. Intraperitoneal injections are made by a cervical approach between the head and forelimbs or retrograde between the tail and hindlimb. Intracardiac injections are dangerous and not recommended.

Etorphine 0.3-2.7 mg/kg IM provided 2 hours of anesthesia, sufficient to biopsy the thyroid gland in Galapagos tortoises (16).

Pentobarbital (2%) 18.2 mg/kg IP produced surgical anesthesia in 80 minutes, lasting 2.5-4 hours (43).

Chlorpromazine 10 mg/kg IM followed by 10 mg/kg pentobarbital by the intracardiac route produced deep anesthesia within 15 minutes, lasting 3 hours. Muscle relaxation was good (69).

Urethane is not recommended because of its variable effects (139). Urethane 2.4 g/kg IV required 135 minutes for induction and lasted over 10 hours (87F).

Ketamine HCl 100 mg IM was used for anesthetic induction, followed by intubation and maintenance with halothane anesthesia for a salpingotomy and cesarean delivery (37).

ANESTHETIZING FISH

Many agents have been used to restrain and anesthetize fish of all sizes. Table 4 lists 15 agents used on a number of species.

TABLE 4. ANESTHETIC AGENTS FOR FISH (105C)

Anesthetic	Concentration*	Anesthetic qualities		
		Induction time (min)	Maintenance	Recovery time (min)
Carbon dioxide	200 ppm	1-2	Good	5-10
Electricity		Immediate	Poor	5-30
Diethyl ether	10-50 ml	2-3	Fair	5-30
Sodium seconal	35 mg	30-60	Good	60+
Sodium amytal	7-10 mg	30-60	Good	60+
Urethane	5-40 mg	2-3	Good	10-15
Chloral hydrate	0.8-0.9 g	8-10	Poor	20-30
Tertiary amyl alcohol	0.5-1.25 ml	10-20	Fair	20-90
Tribromoethanol	4-6 mg	5-10	Fair	20-40
Chlorobutanol	8-10 mg	2-3	Good	30-60
2-Phenoxyethanol	0.1-0.5 ml	10-30	Fair	5-15
4-Styrylpyridine	20-50 mg	1-5	Good	20-30
Methylpentynol	0.5-0.9 ml	2-3	Fair	5-20
Quinaldine	0.01-0.03 ml	1-3	Fair	5-20
MS-222	25-100 mg	1-3	Excellent	3-15

*Per liter of water unless otherwise noted.

Detailed descriptions of these agents and their use in fish are available in two excellent articles (87J, 105C). The optimum concentration of anesthetic to be used must be determined by trial and error in terms of species of fish and temperature and chemical nature of the water.

The most popular agent is tricaine methanesulfonate (MS-222). Dosage is 25-35 mg/liter of water for transporting fish and 50-100 mg/liter of water for deep anesthesia. Induction time is 1-3 minutes, maintenance of anesthesia is excellent, and recovery occurs in 3-15 minutes. Repeated exposure to MS-222 results in only a slight increase

ir drug tolerance. Toxic conditions may result if MS-222 is used in salt water or direct sunlight.

The following technics should be followed when anesthetizing fish (87J, 105C):

1. The vessel containing the anesthetic solution should be chemically inert.

2. The anesthetic solution should be made with water from the same source as that in which the fish are held. A constant temperature should be maintained. Fish cannot tolerate a change of temperature of more than 5°-10°C.

3. The calculated amount of anesthetic should be well mixed into the water. The required concentration should be determined by trial and error for the species of fish to be anesthetized. Testing the anesthetic with stock fish to observe the effects is advisable before the experimental fish are anesthetized.

4. The fish are in a surgical plane of anesthesia when swimming movements subside, respiration is rapid and shallow, and opercular movements are difficult to detect. The fish may be removed from the anesthetic and placed on a wet towel. If gasping and muscle spasms occur, the fish are replaced in the anesthetic solution for a few seconds.

5. Anesthetic overdosage produces cessation of respiration and spasmodic flaring of the opercles at 15-30-sec intervals up to 1-min intervals, at which time all spasms cease and cardiac arrest and death result.

6. Fish may be revived by placing them in fresh water and moving them back and forth slowly to force water over the gills. Recovery occurs within 5-30 minutes after the fish are placed in the fresh water, depending upon length of exposure and concentration of anesthesia.

7. When induction time increases and it is difficult for the fish to enter deep anesthesia, the anesthetic solution is being depleted and should be replaced.

ANESTHETIZING MARINE MAMMALS

The Cetacea (whale, porpoise, dolphin) and Pinnipedia (seal, sea lion, walrus) vary widely in their respiratory and cardiovascular specializations and response to anesthesia.

Cetacea (69, 91, 92, 122H)

Inhalation Anesthesia--The Cetacea are mammals that have developed a completely aquatic life. They have a specialized larynx that allows them to breathe only through a modified nasal passage (blowhole). They have never been successfully anesthetized without complete respiratory

control by positive pressure ventilation. Barbiturate anesthesia without control of ventilation results in death due to asphyxia. Endotracheal intubation and support with a Bird Mark 9 respirator that imitates the porpoise's natural apneustic plateau respiratory pattern (rapid inflation of the lungs and maintenance of inflation for a period of time followed by deflation and rapid reinflation) have enabled successful anesthesia (91, 92, 122H).

Halothane provides excellent anesthesia. Induction is with 3.5% halothane for 5-15 minutes. Surgical anesthesia is maintained at the lowest concentration that inhibits movement of the tail flukes, approximately 1% halothane. During recovery the porpoise is maintained on 40% oxygen and 60% ambient air. The blowhole reflex returns in 15-45 minutes, at which time the porpoise may be extubated (122H).

Injection Anesthesia--Thiopental sodium administered in the tail fluke vein at 10 mg/kg produces 10-15 minutes of very light anesthesia; 15-25 mg/kg produces anesthesia lasting for 10-25 minutes. Recovery of normal respiration requires 1-2.5 hours (122H).

The phenothiazine tranquilizers cause hypothalmic depression and peripheral vasodilatation, altering the heat-conserving peripheral vascular mechanisms and resulting in death. Chlordiazepoxide and diazepam may be safely used in Cetacea (122H).

Succinylcholine is contraindicated in the dolphin because this species lacks plasma cholinesterases (92).

Pinnipedia (43)

The Pinnipedia possess extensive modifications in their respiratory and cardiovascular anatomy and physiology to adapt them for diving. Their slow respiratory pattern with periods of apnea pose problems for inhalation anesthesia. When they dive, their heart rate decreases to 10% normal. Blood flow is primarily to the brain, and a sphincter in the posterior vena cava causes most of the venous blood to pool in the hepatic sinus. When Pinnipedia are frightened, the same diving reflex with breath-holding and pooling of blood may occur; it is possible for an entire IV anesthetic dose to pool in the hepatic sinus until breathing resumes and the vena cava sphincter opens, at which time a high anesthetic concentration is released to the heart (43).

Inhalation Anesthesia--Inhalation anesthesia with halothane has been the most satisfactory for the sea lion. The sea lion is placed in a squeeze cage and administered 0.016 gr atropine/50 kg; anesthesia is induced with halothane by means of a glass hood placed over the head. An endotracheal tube is inserted, and anesthesia is maintained with 0.75%-1.5% halothane. Recovery is rapid, usually within 1 hour after surgery (100).

Injection Anesthesia--Induction of anesthesia by means other than the inhalation route is usually not satisfactory for the sea lion. Succinylcholine and gallamine (neuromuscular blocking agents) produce poor recovery results because of prolonged action. Prolonged recovery

and decreases in body temperature occur with the barbiturate anesthetics. The phenothiazine-derived tranquilizers, peripheral vasodilators, and ganglionic blocking agents markedly depress body temperature. The results of phencyclidine HCl have not been favorable (100).

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